Psychological distress in disease-free breast cancer survivors completing tamoxifen therapy: the contribution of illness and treatment representations to psychological morbidity and research portfolio

Part One (Part Two bound separately)

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Chapter 1: Small-Scale Service Related Project

An analysis of referral characteristics and outcomes referred to an Adult Mental Health Psychology Speciality during a one-year period: comparisons between geographical area and referring agents.

Prepared in accordance with guidelines in the Doctorate in Clinical Psychology Research Training Folder for 'in-service publication'.

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Summary

This retrospective audit aimed to highlight the current demands placed on the existing Adult Mental Health speciality within the Dumfries and Galloway Psychology service in terms of patient and referrer need since the reconfiguration of service provisions and to detail how the needs are currently being met. Specific aims of this audit were; to examine referral characteristics and referral outcomes received during a one-year period (between October 2002 and September 2003), examine service utilisation per geographical area, and to highlight differences in referral characteristics and referral outcome between geographical area and referring agents. Specific referral characteristics examined were: patient characteristics (age and gender) and referring problem (primary problem, chronicity, severity and complexity). Discharge forms, completed by AMH speciality staff as standard, provided the outcome of each referral, detailing reason for discharge, session attendance and subjective clinical judgment of outcome.

A total number of 1303 referrals were referred to the speciality within the one-year period. There were three major referral agents to the AMH speciality, namely, General Practitioners (GP) Community Mental Health Teams (CMHT) and Psychiatric Medical Practitioners (PMP). Referrals were sent for a variety of psychological difficulties however one quarter of referrals were primarily experiencing an anxiety disorder (24.9%) and one quarter with a depressive disorder (24.6%). Attendance varied across referrals, however there were a high percentage of referrals discharged due to non-attendance (37.8%).

Geographically, referrals did not differ in terms of age, sex, attendance or outcome. They did however differ in terms of severity, complexity, and chronicity of referral, which may be a reflection of referring agents in different areas or differences in AMH speciality staff rating

methods. Referrals examined between referral agents did not differ in terms of age, sex, attendance or outcome. They did however differ in terms of severity, complexity, and chronicity of referral, which may be a reflection of primary and secondary caregivers or differences between AMH speciality staff rating methods.

The reliability and validity of outcome ratings are questionable due to being subjective and not calibrated. Discrepancies between outcome frequencies were found and interpretations of data were difficult. The need to revise outcome categories, rating procedures, and to implement guidelines for rating referral characteristics and outcome categories for AMH speciality staff was highlighted, which may reduce future discrepancies between reported data. Staff training to enable consistent and appropriate scoring of discharge forms was recommended. AMH speciality staff inter-rater and intra-rater reliability research, with regards to scoring discharge forms, was also recommended for the department to undertake.

Introduction & Aims

Increasing demands placed on clinical psychology services, at a time when financial resources are severely limited, highlight the need to identify the most effective and efficient ways of providing such services (Kincey & Creed, 1991). This need is now mandatory within all NHS services due to recent government initiatives and legislation that require an evidence-based, high-class service through clinical governance (Department of Health, 1998, 1999). Audit has been recognised as one method where services can evaluate resources efficiently and effectively (Elliot et al., 1994; McPherson et al., 1996). This has resulted in audit becoming an integral and essential process in clinical practice in order to improve the quality of public services. Forsythe & Gallagher (2003) define audit as '...a systematic evaluation of a service resulting in improvements in the quality of care. It should be a cycle of activity involving systematic review of practice, identification of problems, development of solutions, implementation of change and then review again'.

The Dumfries and Galloway Adult Mental Health (AMH) Psychology Speciality is comprised of four teams that are responsible for providing psychological care in a rural setting to four differing geographical areas within Dumfries and Galloway NHS Health Board; Annandale & Eskdale (AE), Nithsdale & Upper Nithsdale (NU), Stewartry (ST), and Wigtownshire (WG). Each area team utilises a wide skill mix in order to provide this care using clinical psychologists, counsellors and psychotherapists[1].

The speciality has undertaken several clinical audits during recent years due to new developments in service provision, initiated with the arrival of the new Director of Psychological services, and the creation of the clinical governance committee within the department. Developments

[1] Throughout this report clinical psychologists, counsellors, and psychotherapists will be referred to 'AMH speciality staff'.

implemented in September 2001, such as a referrer feedback system informing them of client waiting times (unpublished document; Hancock, 1999), Dumfries and Galloway Department of Psychological Services and Research Development Plan 2002/2003), aimed to increase appropriate service utilisation and maximise available resources.

Although audit is a continuous process within the department recent audits have only examined specific variables, such as treatment length and outcome at a macro level (unpublished document; Mackie, 2003), or have been restricted to specialist services such as the 'self-help' project or the evaluative therapeutic outcome project, Clinical Outcomes for Routine Evaluation (CORE). Data was not available within the department detailing referral characteristics or referral outcomes prior to 2001 in order to examine if the developments had an impact on service utilisation and provision. It was therefore deemed necessary to review service provision at present, at macro and micro levels, between geographical areas and referring agents in order to have an accurate baseline of current service provision.

A review of this type aims to highlight current demands placed on the existing service in terms of patient and referrer need and will detail how that demand is currently being met. This information can inform future developments to increase service responsivity through a local needs-led approach, thus increasing service efficiency. Specific aims of this audit are therefore:

- To examine referral characteristics and referral outcomes received during a one-year period to the AMH speciality in the Dumfries and Galloway NHS Health Board.
- To examine service utilisation per geographical area in terms of attendance rates.
- To highlight differences in referral characteristics and referral outcome between geographical area and referring agents.

Methodology

This was a retrospective audit of referrals received to the AMH speciality during a one-year period (to minimise the effects of seasonal variation) between October 2002 and September 2003. The only exclusion category employed was if the client had not been discharged by 6th May 2004. Data was extracted from the Psychology Management System (PMS), where data is routinely collected from AMH speciality staff using the standard discharge form (see Appendix 1.1), which every referral received to the service is rated on for the purposes of service audit. Data was exported into a statistical package for windows (SPSS v11.0) for examination. Patient identifiers were removed from the data set and each patient was allocated an identity number in order for the data to be anonymous. Referral agent identifiers were also removed. Missing data was identified through frequency reports and was recovered through case file searches.

Referrals were examined in terms of referral characteristics and referral outcomes for the whole AMH speciality and were also examined between geographical areas and referral agents. Specific referral characteristics examined were patient characteristics (age and gender) and referring problem (primary problem, chronicity, severity and complexity). Referrals are rated by AMH speciality staff on standard discharge forms using either information gathered during assessment or subsequent sessions, or with the detailed information provided by the referring agent at time of referral if assessment sessions were not attended by, or offered to, patients. Umbrella categories of disorders/difficulties experienced by clients, as rated by AMH speciality staff members (using the same method detailed above), were also taken from individual discharge forms currently used within the department. Fifteen umbrella categories of disorders/difficulties are used encompassing over 80 diagnostic categories; Depressive mood, anxiety disorder, obsessive compulsive, personality problems, sexual problems, family/relationship problems, social functioning,

adjustment difficulties with life events, eating disorder, sleep disorder, addiction, physical health problem, employment difficulties, intellectual impairment, and psychosis.

Discharge forms also provided the outcome of each referral, completed by AMH speciality staff as standard, detailing session attendance, reason for discharge (planned discharge, re-referral, non-attendance etc), and subjective clinical judgment of outcome (e.g., improved, no change).

The data were examined for skewness and kurtosis. Data were not normally distributed therefore non-parametric statistics were employed. Data were examined using frequencies and cross tabulation. Mann Whitney-U tests were employed to test for significant differences between geographical area/referring agents and continuous variables, such as age or number of sessions attended. Referral characteristics and outcomes were examined for significant differences between geographical area/referring agents using Chi-square tests, as data are regarded as nominal rather than ordinal/interval due to ratings being subjective and categorical, using probability levels calculated by the Bonferroni test on repeated post-hoc analyses (Brace et al., 2003).

Results

AMH Speciality: Referral Characteristics

A total number of 1303 adult mental health cases were recorded as being referred between 1st October 2002 and 30th September 2003 and subsequently discharged by 6th May 2004. The mean age of the sample was 37.14 (SD=11.71), with ages ranging from 17 to 64, and 65.5% (853) of the sample was female and 34.5% (450) was male.

Referring Agents

There were three major referral agents to the AMH speciality, namely, General Practitioners (GP) (n=962, 73.8% of all referrals), Community Mental Health Teams (CMHT) (n= 124, 9.5%) and Psychiatric Medical Practitioners (PMP) (n=117, 9.0%). The twelve remaining referral agents consisted of other mental health related professionals (n=100, 7.7%).

Problems Experienced

Approximately one quarter of the total number of referrals received (n=1303) were assessed, by AMH speciality staff on discharge forms, as primarily experiencing an anxiety disorder (n=324, 24.9%), one quarter a depressive disorder (n=320, 24.6%), 10.1% (n=132) with family or relationship difficulties and 8.5% (n=111) with difficulty adjusting to life events (table 1). Of the total number of referrals (n=1303) sent to the department a number of referrals (n=164, 12.6%) did not have a specific primary diagnosis rating due to clients dropping out of the speciality before a full assessment of presenting difficulties was completed or because of limited referral information being provided by referral agents for clients that did not attend the AMH speciality prior to discharge (due to not attending or not being offered an appointment).

TABLE 1: Umbrella term of specific primary diagnosis

	Frequency	Percent
Depressive Mood	320	24.6
Anxiety Disorder	324	24.9
Obsessive Compulsive	10	0.8
Personality Problems	56	4.3
Sexual Problems	17	1.3

Family/Relationship Problems	132	10.1
Social Functioning	53	4.1
Adjustment to Life Event	111	8.5
Eating Disorder	12	0.9
Sleep Disorder	4	0.3
Addiction	16	1.2
Physical Health	40	3.1
Employment Difficulties	33	2.5
Intellectual Impairment	3	0.2
Psychosis	8	0.6
Information not provided by referring agent	164	12.6
Total	1303	100.0

Problem Severity

Of the total number of referrals (n=1303), AMH speciality staff rated client problem severity as mild (n=216, 16.5%), moderate (n=557, 42.7%), or severe (n=282, 21.6%). Remaining referrals not rated (n=249, 19.1%) were due to non-attendance (first or subsequent appointments) or limited referral information being provided by the referring agent at time of referral.

Problem Chronicity

Of the total number of referrals (n=1303), chronicity was found to be mainly over one year (n=653, 50.1%), between six or twelve months (n=283, 21.7%), or less than six months (n=100, 7.7%). Chronicity was unable to be rated in 267 cases (20.5%) due to non-attendance (first or

subsequent appointments) or limited referral information being provided by the referring agent at time of referral.

Problem Complexity

Of the total number of referrals (n=1303) the complexity of problem varied between; 'high degree' (n=128, 9.8%), 'moderate' (n=419, 32.2%), 'low degree' (n=290, 22.3%), and 'not complex' (n=230, 17.7%). Complexity was not rated in 236 cases (18.1%) due to non-attendance (first or subsequent appointments) or limited referral information being provided by the referring agent at time of referral.

Referral Characteristics: Discrepancies in Reported Data

Particular frequencies and percentages of referrals reported above differ between subsections, for example, severity (19.1%; n=249), complexity (18.1%; n=236) and chronicity (20.5%; n=267). It would be expected that the number of cases 'not rated' would be consistent across referral characteristic categories, however, it should be noted that these numbers do not solely represent clients that have been seen by AMH speciality staff and staff may have rated clients problem severity by using information provided by the referring agent prior to discharge. Thus, some referral letters may have more detailed information specifying the complexity of the problem but not enough relating to the chronicity or severity of the problem (and vice versa) preventing the AMH speciality staff member to rate a particular category. Therefore, enough information was obtained through assessment/subsequent sessions or enough information was provided by the referring agent for AMH speciality staff to rate problem severity in 1054 referrals (80.9%) problem complexity for 1067 referrals (81.9%) and problem chronicity in 1036 referrals (79.5%).

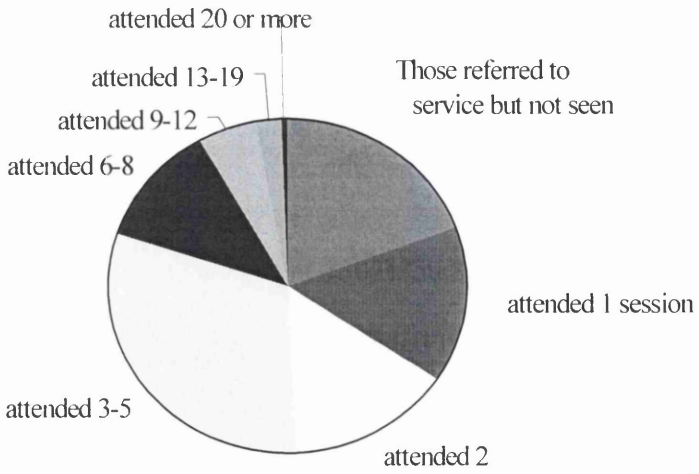
The number of referrals 'not rated' on a characteristic should not be deduced as non-attendance to allocated appointments. Although discrepancies between data can be explained in general terms it is unclear which referrals were not rated and why e.g., were they transferred to another area prior to being seen? This highlights gross difficulties with the rating and scoring of discharge forms and the inconsistency of rating practices between AMH speciality staff.

AMH Speciality: Referral Outcomes

Attendance

Of the total number of referrals received (n=1303), 50.8% (n=662) attended three or more sessions, 15% (n=195) attended one, 14.7% (n=192) attended two, and 19.5% (n=254) did not attend at all prior to discharge (diagram 1).

Diagram 1. Number of sessions attended for all referrals received



Frequencies reported for the number of sessions attended by referrals sent to the service, are inclusive of referrals that were assessed on receipt of referral to be either appropriate or inappropriate to the area/speciality. Therefore, although 19.5% (n=254) of referrals did not attend the speciality at all prior to discharge this percentage includes referrals that did not attend appointments allocated to them, referrals that were assessed on receipt as not appropriate, and referrals that 'opted out' of the speciality.

Between one and two percent of referrals were not offered a locally based appointment, whether at the department or within a GP practice or health centre, requiring clients to travel longer distances to attend appointments.

Reason for Discharge

Of the total number of referrals (n=1303) received, main reasons for discharge were found to be; failure to attend during treatment (n=360, 27.6%), treatment completed (n=247, 19.0%), and problems resolved (n=175, 13.4%). The proportion of referrals recorded as 'never seen' (n=133, 10.2%), as the given reason for discharge, is the proportion of clients that did not attend any appointments that were allocated to them. Only 3.1% (n= 41) of referrals 'opted out' for their first appointment whereby declining to be seen by a member of the department when near the top of the waiting list (Table 2). It is unclear how many sessions were attended by referrals prior to discharge in the various subcategories given, such as 'transfers' or 'failed to attend'.

TABLE 2. Reason for Discharge

	Frequency	Percent
Opted out	41	3.1
Died	2	.2
Failed to attend	360	27.6
Never seen	133	10.2
No further improvement possible	126	9.7
Parental/client request	90	6.9
Problems resolved	175	13.4
Transfer to another clinician	41	3.1
Transfer to another area	16	1.2
Transfer to another agency	36	2.8
Treatment complete	247	19.0
Unable to attend	23	1.8
Inappropriate referral	1	0.1
Clinician did not report	12	0.9
Total	1303	100.0

Subjective Rating of Referral Outcome

Of the total number of referrals sent to the AMH speciality (n=1303) nearly one half of clients referred were rated by AMH speciality staff at discharge as 'improved' (n=620, 47.5%), 11.2% (n=146) 'unchanged', and 0.6% (n=7) as 'deteriorated'. The remaining 530 referrals (40.7%) were not rated on a subjective outcome category by AMH speciality staff due to never being seen (n=225, 17.3%), failure to attend (n=89, 6.8%), only seen once (n=193, 14.8%) or 'other' (n=23,

1.8%). When excluding referrals not allocated to an outcome category due to these reasons, 80.1% of referrals that participated in therapy with AMH speciality staff were discharged and rated as having made either much, moderate, or slight improvement.

Referral Outcomes: Discrepancies in Reported Data

Frequencies and percentages of reported outcomes reported also differ between subsections. For example, attendance frequencies showed that 254 (19.5%) referrals did not attend the speciality at all prior to discharge. However, ratings for the subjective outcome reported that 225 (17.3%) referrals were never seen whereas 'reason for discharge' reported that 133 (10.2%) referrals were never seen.

The discharge form does not utilise the full variation of outcome categories required to be rated within the subjective outcome subsection, for example, referrals that were 'unable to attend' or 'transferred' can only be rated as 'never seen', 'failed to attend', or 'other' within the 'reason for discharge' section. This creates significant difficulties to track the outcome for referrals (i.e., what proportion of referrals that were never seen were those transferred to another area, service, or clinician, died, opted out, or were unable to attend prior to discharge?). Therefore it is advised that only the frequencies for improvement or deterioration reported in the subjective outcome section should be utilised as the 'failed to attend', 'never seen', 'only seen once' and 'other' frequencies are indescribable of referral populations.

The most accurate and reliable subsection to refer to when reporting non-attendance by referrals is 'reason for discharge' as it has a full breakdown of the available referral outcomes. The breakdown records referrals that were transferred out with the service, opted out etc. Therefore

categories such as 'never seen' and 'failed to attend' can be reliably reported for referrals that did not attend the speciality prior to discharge due to non-attendance of allocated appointments (n=133; 10.2%) and for referrals that failed to attend during treatment sessions (n=360; 27.6%). Therefore the number of referrals that were discharged from the speciality due to not attending appointments that were allocated to them was 37.8% (n=493).

In conclusion, subsections detailing referral outcomes are rated independently of each other on the discharge form and discrepancies between frequencies can be explained by overlapping sub-categories on the discharge form, rating errors, or inconsistencies between AMH speciality staff ratings. This highlights a significant problem with the current format and rating of the discharge form.

Geographical Area: Referral Characteristics & Outcome

AE* received 493 referrals (37.8%); NU received 555 (42.6%); ST received 125 (9.6%); and WG received 130 (10.0%) during the one-year period. There were no significant differences found between geographical areas and the gender of referral (x^2=0.318, df=3, p=0.957, two-tailed) using a Chi-square test. Using a series of Mann-Whitney-U tests no significant differences were found between geographical areas and the age of referrals (see Appendix 1.2, table 1). Compared to other areas, where GPs were the main referral agent (86.2%, 71.5%, 75.2%), WG received more referrals from CMHT (51.5%) than GPs (35.4%).

In WG there was a higher percentage of referrals for depressive disorders (38.5%) compared to other areas (22.5%, 22.9%, 25.6%) and also for anxiety disorders (27% compared to 21.5%,

* AE=Annandale & Eskdale; NU = Nithsdale & Upper Nithsdale; WG= Wigtownshire; ST= Stewartry

23.2%, 24.8%). The majority of referrals from areas out with the department attended their psychology appointments in a local health centre or GP practice (Table 3) reducing the time required to travel to an appointment at the department.

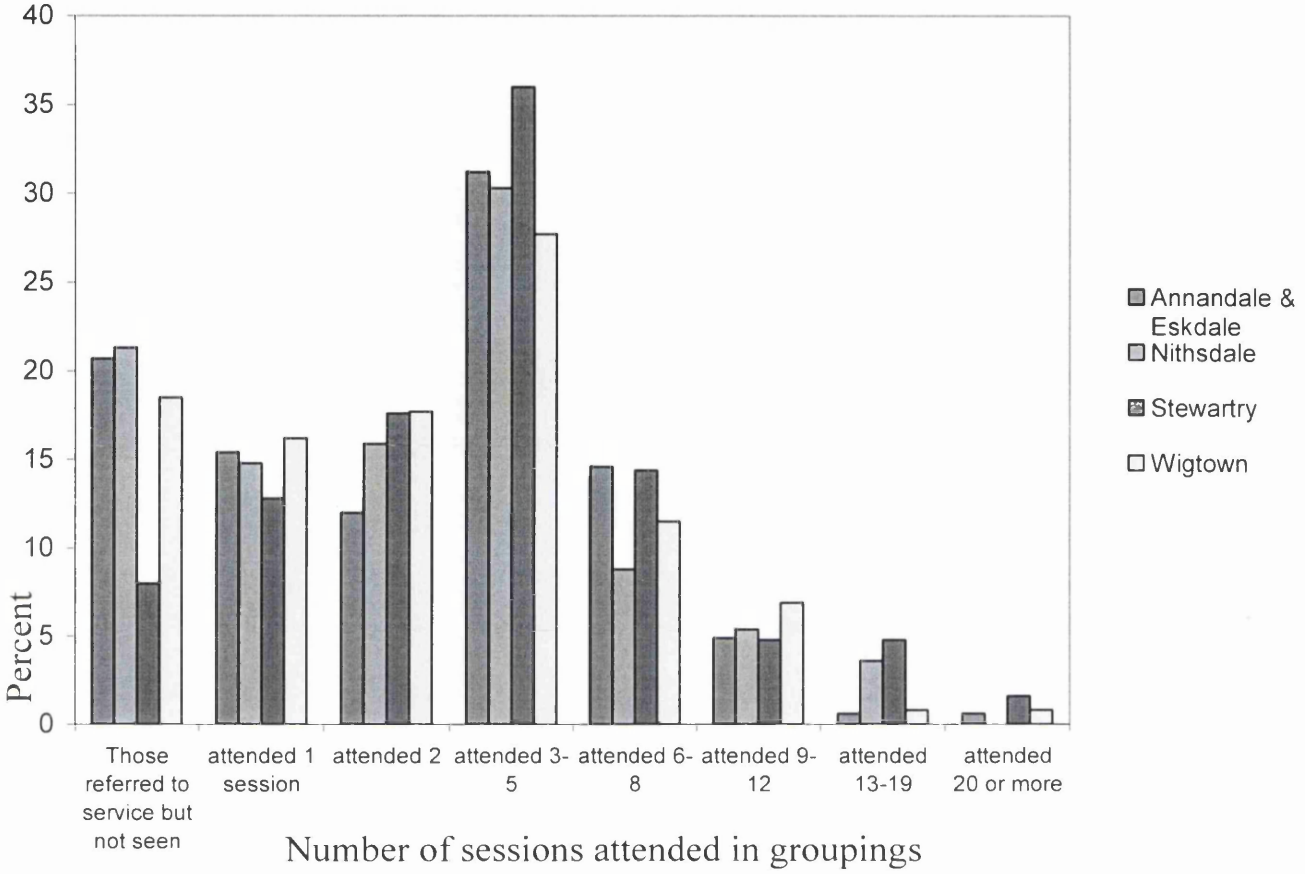
Tabe 3. Location of Appointment per Geographical Area

		Area				Total
		AE*	**NU**	**ST**	**WG**	
Psychology Dept	Count	22	392	17	3	434
	% within Area	*4.5%*	*70.6%*	*13.6%*	*2.3%*	*33.3%*
Health center/GP surgery	Count	461	159	107	126	853
	% within Area	*93.5%*	*28.6%*	*85.6%*	*96.9%*	*65.5%*
Hospital/Day Hospital	Count	9	4	-	1	14
	% within Area	*1.8%*	*0.7%*	-	*0.8%*	*1.1%*
Hone Visit	Count	1	-	1	-	2
	% within Area	*0.2%*	-	*0.8%*	-	*0.2%*
Total	Count	493	555	125	130	1303
	% within Area	*100%*	*100%*	*100%*	*100%*	*100%*

Using a series of Mann Whitney-U tests attendance did not differ significantly between areas (see Appendix 1.3, table1). However, ST had the lowest first session DNA rate (8%) compared to other areas, 18.5%, 20.7% and 21.3% (Diagram 2).

** AE=Annandale & Eskdale; NU = Nithsdale & Upper Nithsdale; WG= Wigtownshire; ST= Stewartry

DIAGRAM 2. Attendance by Geographical Area



Using Chi-square tests relationships were found between geographical area and AMH speciality staff ratings of severity (x^2=21.798, df=6, p=<0.001), chronicity (x^2=42.266, df=6, p=0.000) and complexity (x^2=66.358, df=9, p=0.000) of referrals. Post-hoc Chi-square analyses were employed to ascertain which geographical areas differed significantly, using the Bonferroni procedure to calculate significance levels. Statistical differences found between geographical areas, in terms of severity, chronicity and complexity, can be viewed in table 4.

TABLE 4. Referral Characteristics: significant differences between geographical area

Referral Characteristic	**Area***	**Statistical Difference**
Severity	AE vs. ST	x^2=18.481, df=2, p= 0.000
Chronicity	NU vs. AE	x^2=27.479, df=2, p= 0.000
	WG vs. AE	x^2=27.479, df=2, p= 0.000
	ST vs. AE	x^2=27.479, df=2, p=0.000
Complexity	ST vs. AE	x^2=31.181, df=3, p= 0.000
	ST vs. NU	x^2=26.200, df=3, p= 0.000
	ST vs. WG	x^2=42.666, df=3, p= 0.000
	NU vs. WG	x^2=26.200, df=3, p= 0.000
	AE vs. WG	x^2=31.181, df=3, p= 0.000

The statistical difference found between ST and AE, in terms of severity of referral, highlighted that both areas rated approximately half of their referrals as moderately severe however the majority of remaining referrals within ST are rated as being of mild severity whereas in AE the remaining majority are rated as severe. Within ST the majority of referrals were rated as being either mild (30.6%) or moderately severe (55.6%) whereas in AE the majority were rated as being either moderately severe (52.9%) or severe (31.0%). This suggests that AMH speciality staff working in ST rate the majority of their referrals as less severe than AE.

In terms of chronicity, AE differed from other geographical areas where the majority of referrals from NU (69%), WG (77.4%), and ST (66.9%) were rated as having their difficulties for over one

* AE=Annandale & Eskdale; NU = Nithsdale & Upper Nithsdale; WG= Wigtownshire; ST= Stewartry

year compared to only 50% of AE referrals. AE had a higher percentage of referrals (37.0%) rated as having their difficulties for 6-12 months compared to the other three geographical areas (<22.8%).

Within ST[•] the majority of referrals were rated as being not complex (41.1%) compared to the other geographical areas where a more evenly spread of complexity was found, except from WG where the majority of referrals were rated as being of moderate complexity (62.4%).

Outcome as rated by AMH speciality staff on discharge, did not differ significantly between geographical areas (x^2=5.476, df=3, p=0.140) using a Chi-square test. In relation to reason for discharge, WG had the highest percentages for 'failed to attend' (33.8%), much improved (23.8%), parental/client request (13.1%), and the lowest percentage for 'did not opt-in' (1.5%). ST had the lowest number of referrals being discharged as 'unchanged' (4.8%) compared to other areas (AE =13.3%; NU= 10.5%; WG= 13.1%). AE and ST had higher rates for discharging due to problems having 'resolved' (16.4%, 16.8%).

Referring Agent: Referral Characteristics & Outcome

Using a Chi-square test no significant differences were found between referring agents and the gender of referral (x^2=3.201, df=2, p=0.202, two-tailed). Using a series of Mann-Whitney-U tests no significant differences were found between referring agents and the age of referrals (see Appendix 1.2, table 2). CMHT and PMP[•] referrals were mainly for depressive disorders (41.9%; 39.3%) whereas GP referrals varied to a greater degree with the highest percentage being for

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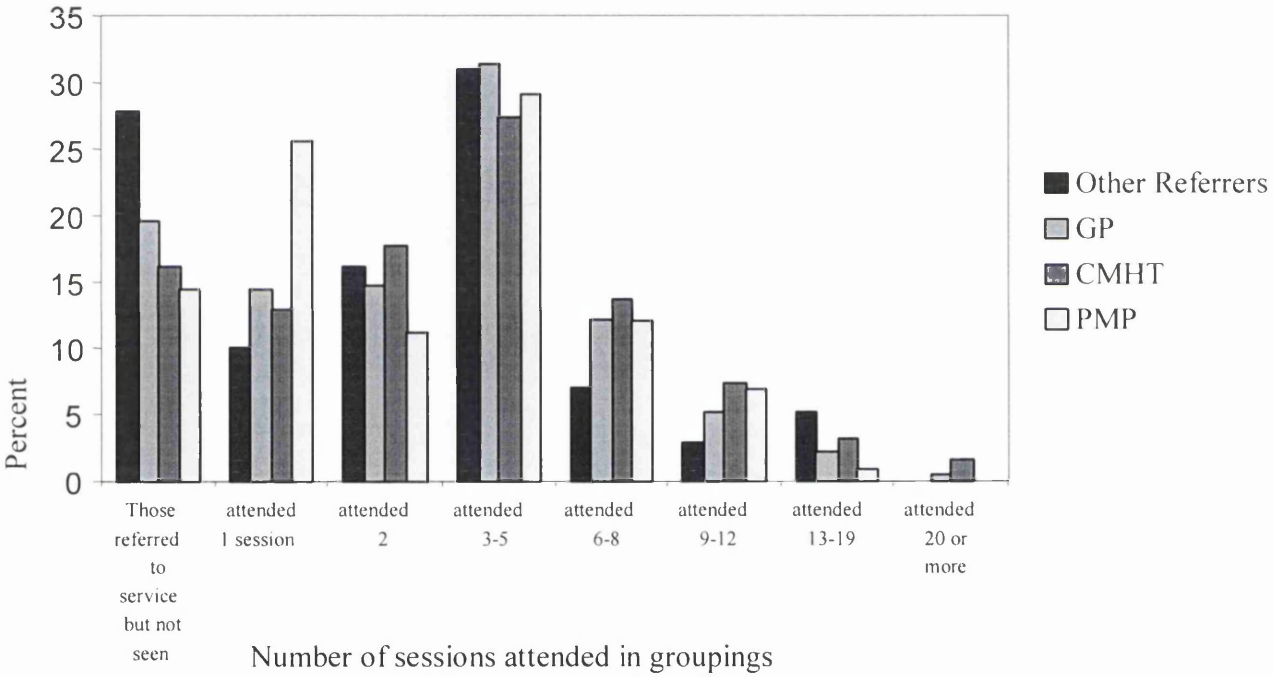
[•] AE=Annandale & Eskdale; NU = Nithsdale & Upper Nithsdale; WG= Wigtownshire; ST= Stewartry

[•] PMP= Psychiatric Medical Practitioner; CMHT= Community Mental Health Team; GP= General Practitioners

anxiety related disorders (26.9%) and family/relationship problems (11.4%). There were no significant differences in session attendance between the three main referral agents (see Appendix 3, table 2), however GP referrals had a higher first session DNA rate (19.6%) compared to CMHT (16.1%) and PMP (14.5%). Approximately one third of referrals from each referral agent, GP (31.5%), CMHT (27.4%), and PMP (29.1%), attended 3-5 sessions prior to discharge (Diagram 3).

DIAGRAM 3. Number of Sessions Attended per Referring Agent



There was a relationship found between referring agent and AMH speciality staff ratings of severity (x^2=35.981, df=4, p=0.000), chronicity (x^2=28.242, df=4, p=0.000), and complexity (x^2=69.475, df=6, p=0.000) of referrals using Chi-square tests. Post-hoc Chi-square analyses were used to ascertain which referring agents differed significantly, using the Bonferroni procedure to

calculate significance levels. Statistical differences found between referring agents, in terms of severity, chronicity, and complexity, can be viewed in table 5.

TABLE 5. Referral Characteristics: significant differences between referring agents

Referral Characteristic	Referral Agent*	Statistical Difference
Severity	GP vs. PMP	x^2=33.449, df=2, p= 0.000
Chronicity	GP vs. CMHT	x^2=21.900, df=2, p= 0.000
	GP vs. PMP	x^2=21.900, df=2, p= 0.000
Complexity	GP vs. CMHT	x^2=48.108, df=3, p= 0.000
	GP vs. PMP	x^2=48.108, df=3, p= 0.000

The majority of referrals received by GPs were rated as being either mild or moderately severe (76.5%) whereas the majority of PMP referrals were rated as being either moderately severe or severe (92.0%). No significant differences were found between CMHT referrals and GP referrals in terms of severity as rated by AMH speciality staff members.

In terms of chronicity, GPs differed from other referring agents. The majority of referrals from CMHTs (81.7%) and PMPs (72.8%) were rated as having their difficulties for over one year compared to only 57.8% of GP referrals. Additionally, GPs had a larger percentage of referrals (31.2%) being rated as having their difficulties for 6-12 months compared to CMHTs (13.5%) and PMPs (18.4%).

* PMP= Psychiatric Medical Practitioner; CMHT= Community Mental Health Team; GP= General Practitioners

The majority of CMHT referrals were rated as being moderately complex (64.2%). Other referring agents were found to have a more even spread of complexity, although a higher percentage of GP referrals were rated as not complex (25%) compared to CMHT referrals (8.5%) and PMP referrals (10.7%). Additionally, more PMP referrals were rated as having a high degree of complexity (22.3%) compared to CMHT referrals (16.0%) and GP referrals (8.8%).

PMP and CMHT referrals did not differ significantly in terms of severity, chronicity, or complexity. AMH speciality staff ratings of GP referrals, in comparison to CMHT and PMP referrals, were less severe, less chronic, and were mostly rated as either 'not complex' or having a 'low degree' of complexity (45.3%).

Outcome, as rated by AMH speciality staff on discharge, did not differ significantly between referring agents (x^2=8.511, df=2, p=0.140) using a Chi-square test. However, PMP had a higher percentage of referrals being discharged due to 'no further improvement possible' compared to CMHT and GP referrals. PMP had the lowest percentage of referrals being discharged as 'much improved' (10.3%) and a higher percentage of referrals being rated as 'unchanged' (14.5%) compared to GPs (18.3%; 9.9%). CMHTs had the highest percentage of referrals being discharged as 'much improved' (19.4%) and 'unchanged' (17.7%). Over one quarter of referrals received from PMPs (26.5%; n=30) were only seen once for assessment prior to discharge.

Discussion

The reliability and validity of AMH speciality staff ratings of outcome are questionable due to being subjective and not calibrated. More importantly however, categories used to rate referral

outcomes on the discharge form grossly overlap, creating difficulties in obtaining an accurate picture of referral outcomes. For example, it is unclear why referrals were 'never seen' or 'failed to attend' and why outcome was not subjectively rated. Additionally, it appears that AMH speciality staff ratings are inconsistent when defining 'failure to attend' and 'never seen' inhibiting an accurate reflection of referral outcomes.

Although significant concerns surrounding the reliability and validity of discharge forms has been raised some findings are interesting to note. A high proportion (37.8%) of referrals were discharged from the AMH speciality due to non-attendance (taken from 'reason for discharge' ratings; 'failure to attend' and 'never seen'). This percentage includes clients that did not attend the service at all (never seen; 10.2%) despite being assessed on receipt of referral as an appropriate referral, together with clients who stopped attending the service during therapy (failure to attend; 27.6%). The impact of travelling in a rural area on attendance rates was unlikely to be an issue as approximately 98% of referrals were offered local appointments; therefore locality cannot be posited as a factor contributing to non-attendance. Nevertheless, first session non-attendance rate (10.2%) in the Dumfries and Galloway AMH speciality was found to be lower in comparison to other psychological services (11%-20%) (Trepka, 1986; Startup, 1994; Murray & Hewitt, 1996). Additionally, clients that stopped attending the AMH speciality during therapy (27.6%) was found to be similar to other psychological services (25-30%) (Weighill et al., 1983; Madden & Hinks, 1987; Fadrid & Alport, 1993; Hughes, 1995; Startup, 1995).

Reasons for referral were similar to those of other services (Forsythe & Gallacher, 2003; Telford et al., 1996). Referrals varied in their severity, chronicity, and complexity. A majority of referrals however were rated as either moderate or severe and having their difficulties for over one year.

Despite the variety in referral characteristics, over 80% of referrals seen by AMH speciality staff were discharged as having improved to some extent.

Comparison between Geographical Areas

Age, sex, and attendance rate did not differ between geographical areas. Statistical differences were found between areas in terms of severity, chronicity and complexity of problem. Wigtownshire received more referrals from CMHT than GPs, compared to other areas, which may be a reflection of their GP referral pattern alone. Nevertheless, this difference may be responsible for the significantly higher percentage of more chronic and complex referrals that Wigtownshire received compared to other areas. Additionally, the higher percentage of depressive and anxiety related referrals in this area could be a result of the CMHT referring cases where medicated management is not appropriate for whole problem management, thus utilising psychological intervention for more complex cases.

The statistical differences found between Annandale & Eskdale and other areas in terms of referral chronicity could be a result of unreliable ratings, differing waiting times between areas or GP referral patterns. GPs within Annandale & Eskdale may be more receptive in detecting psychological difficulties earlier than GPs in other areas or have a more favourable attitude to psychological interventions and are thus more amenable to refer to psychological services.

Statistically Stewarty was found to differ significantly from all other areas in terms of referral complexity. The majority of referrals were rated as less complex, compared to other areas. Reasons for this difference are not explicit, as the chronicity of Stewarty referrals were similar to other areas, and severity ratings lower than Annandale & Eskdale. Although statistically

significant, differences may not be clinically significant and highlights reliability issues of subjective ratings of referral characteristics between areas i.e., it is unclear whether one AMH speciality staff member's subjective rating of low severity is the same as another's.

In conclusion, each area team of the AMH speciality provides psychological care to clients with difficulties with varying levels of severity, chronicity and complexity. Although statistically it appears that some areas differ in terms of their referral characteristic populations, this may be an artefact of AMH speciality staff ratings differing rather than the referral populations.

Comparison between Referral Agents

Age, sex, attendance, and outcome did not differ between referral agents. Statistical differences were found between referral agents in terms of severity, chronicity and complexity of problem. The majority of GP referrals were rated as less severe than PMP referrals, less chronic than CMHT and PMP referrals, and were found to have a higher percentage of low complexity referrals than PMP or CMHT referrals. This could be a reflection of primary versus secondary service referrals where CMHT and PMP referrals would be expected to be more severe, complex and chronic due to clients having existing contact with mental health services. Nevertheless, statistical differences do not necessarily reflect a clinical difference in client populations referred by differing referring agents to the AMH speciality, as reliability issues regarding ratings of referral characteristics must also be taken into account during interpretation. It is interesting to note that PMP and CMHT referrals did not differ in referral characteristics but did in referral outcome (although not significantly) where CMHT referrals had a higher percentage of referrals being discharged with improvement and over a quarter of PMP referrals were discharged after one assessment session.

This may reflect a need to revise guidelines of referral suitability and highlight a training need of Psychiatric Medical Practitioners regarding referral suitability to the AMH speciality.

The higher percentage of referrals from CMHT discharged as 'unchanged' and PMP referrals being discharged after one assessment session may reflect the severity, chronicity and complexity of problems that represent cases not amenable to psychological intervention. It may also be the case that CMHTs are more familiar with the clients they refer, of psychological intervention, and the treat-ability of problems, resulting in better treatment outcomes. However, the large percentage of referrals found to be discharged as 'unchanged' and 'deteriorated' from CMHTs and PMPs may also represent a proportion of 'last chance' referrals to psychological services where secondary services have not been able to make an impact on the referral's presenting problem therefore psychology seems the other alternative.

In conclusion, clients referred by the three main referring agents have been rated to have difficulties with varying levels of severity, chronicity and complexity. For example, GPs have been rated by AMH speciality staff to refer less severe, chronic and complex referrals than secondary mental health service providers i.e., CMHTs and PMPs. Although this difference may be understandable, in terms of referral characteristics, this may also be an artefact of AMH speciality staff ratings differing rather than the referral agent's client population.

Recommendations for Service Provision and Future research

- The current discharge form employed by the speciality should be extensively reviewed and adapted to address some of the inconsistencies highlighted earlier in this report. Specifically

the discharge form needs to incorporate the variability of 'outcomes' available to referrals. For example, the subjective outcome section should include the additional 'reason for discharge' categories such as 'transfer to another clinician'. This would minimise the confusion surrounding discrepancies between frequencies reported for 'never seen' and 'failure to attend' between outcome categories. Categories such as 'never seen' and 'failure to attend' should be broken down into more definable categories such as 'never seen – did not attend allocated appointment' or 'failed to attend – after 1/2/3/4 sessions'.

- Outcome categories rated by AMH speciality staff are presently subjective and should have defining criteria to ensure consistency across geographical area/AMH speciality staff member. This should limit future results being unclear due to subjective measures. Additionally, research investigating the inter-rater reliability and intra-rater reliability of AMH speciality staff ratings of referral characteristics may also be useful following adaptations to the discharge form.
- Staff training demonstrating how to rate referrals and explanation of categories available for rating should be incorporated into speciality workshops or inductions to ensure consistency of rating.

Dissemination of Findings

The findings presented in this audit will be presented to the Director of Psychological Services, speciality staff, and management staff of the Department of Psychological Services and Research in August 2004. This report will also be sent to the department of Clinical Effectiveness in Dumfries and Galloway for general staff access.

The Director of Psychological Services may present select results to Senior Management Members of the Dumfries and Galloway NHS Health Board.

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Chapter 2: Systematic Literature Review

Postoperative cognitive dysfunction in Older Adults undergoing non-cardiac surgery: Incidence, Risk, and Features.

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Prepared in accordance with requirements for submission to Neuropsychology Review (see Appendix 2.1)

Submitted in partial fulfilment of the requirements for the Degree of Doctorate in Clinical Psychology.

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Abstract

There is concern that older patients may be at risk of 'Postoperative Cognitive Dysfunction' (POCD) arising from surgical procedures. The purpose of this review was to systematically review the quality of the evidence for such impairment following general anaesthesia, as clinicians should be aware of the incidence, risk, and features associated with POCD. The search strategy involved a computerised search of all major health care databases using key terms to identify papers suitable for review. A total of eight papers were retained for review. Criteria assessing methodological quality was tailored to the investigation of POCD using 'Statement of Consensus' and 'SIGN' guidelines. Whilst a number of reported incidences appear reliable, risk factors and features contributing to POCD remain unclear due to methodological limitations of the current literature. High quality studies found POCD to occur postoperatively in 14.3% - 28.5% of older adults at approximately one week, 8.1% - 20.4% of older adults at three months, and to persist in <1% at 1-2 years following surgery. Risk factors identified with POCD at one week were increasing age, hospitalisation, little education, and postoperative complications and infections. Risk factors associated with cognitive decline at three months were increasing age and benzodiazepines before surgery being protective. Risk factors associated with POCD at 1-2 years were increasing age, POCD at one week, and infection within the first three postoperative months. Limitations of the current literature are discussed and suggestions for future research are proposed.

Keywords: Postoperative cognitive dysfunction (POCD), older adults, risk factors.

Background

Population

The Scottish Executive has estimated that between the year 2000 and 2031 the number of people over the age of 65 is expected to increase from 787,000 to 1,200,000 and those over 85 years from 84,000 to 150,000 [Scottish Executive, 2002]. Such ongoing changes in the demographic characteristic will represent a general increase in the proportion of older adults leading to an assumed growth in the numbers presenting to hospital for surgery. Changes of this nature are already being evidenced within healthcare settings. For example, the number of older adults receiving hip replacement surgery has doubled in the period from 1978 to 2002 [Scottish Executive, 2002]. The reasons for increased life expectancy of older adults are complex and likely include cultural and societal changes as well as improvements in healthcare, medical, and surgical interventions. Whilst modern anaesthetic techniques and surgical methods have improved survival rates, there is however concern that older patients may be more vulnerable to cognitive impairment arising from surgical procedures. The purpose of this review is to determine the quality of the evidence for such impairment.

POCD

Cognitive decline following surgical procedures is known as 'Postoperative Cognitive Dysfunction' (POCD) which is a term used to convey a mild neurocognitive disorder [Bekker & Weeks, 2003]. Although not referenced in the American Diagnostic and Statistic Manual of Mental Disorders, Fourth Edition-TR, it is considered to be a *cognitive disorder not otherwise specified,* characterised by impairment of memory, concentration, executive functioning, disturbance in attention or speed of information processing, perceptual-motor abilities, or language comprehension [Moller, 1997]. It is distinct from delirium and other confusional states that may occur in response to medical treatment and can be differentiated from the acute effects of medication in the immediate postoperative period

[Silbert et al. 2001]. It presents as less severe than dementia and has been reported to have socioeconomic implications encompassing a loss of independence, need for extra nursing care, and a high discharge rate to long-term care [Bekker & Weeks, 2003]. Several authors have also proposed a relationship between postoperative cognitive dysfunction and subsequent dementia [Newman et al. 1995; Ritchie et al. 1997; Roman et al. 2002; Pfitzenmeyer et al. 2001]. The potential negative and significant outcomes arising from surgery has therefore been of great interest to researchers and clinicians alike, and has even prompted the development of an 'International Study of Postoperative Cognitive Dysfunction' (ISPOCD) group, to examine POCD further.

Early Research on POCD

Numerous iatrogenic variables have been proposed as potentially contributing to the development of POCD including factors within the preoperative [Chung et al. 1989; Crul et al. 1992; Berggren et al. 1987], intra-operative [Chung et al. 1987; Flatt et al. 1984; Hole et al. 1980; Dodds & Allison, 1998] and postoperative period [Smith et al. 1991, Berggren et al. 1987, Katz & Fagraeus, 1990, Edwards et al. 1981, Rosenberg & Kehlet, 1993]. A review of earlier research stated that exposure to general anaesthesia can be a cause of short-term and long-term cognitive impairment and was a common complication in elderly patients undergoing cardiac and non-cardiac surgery [Dodds & Allison, 1998], but concluded that causes were difficult to establish. However, numerous methodological limitations have been shown in earlier studies of POCD [Rasmussen, et al. 2001; Dijkstra & Jolles, 2002] which have compromised the generalisability of the findings.

Methodological Limitations

Dijkstra & Jolles [2002] noted such methodological limitations as being the selection of inappropriate neuropsychological assessments, unresolved practice effects, variable definition of cognitive decline, and ecological validity of assessments. The selection bias of patients pertains to

the exclusion of those with pre-existing cognitive deficits so few studies are representative of an older adult population. It has also been highlighted that anxious, depressed, or fatigued patients are more likely to refuse participation, which may result in vulnerable populations who might be more susceptible to cognitive decline being excluded from analyses, thus reducing the apparent incidence of POCD in older adult populations.

Methods to define cognitive decline in earlier research typically compare mean group performances. This has been suggested to artificially reduce the apparent incidence of POCD in older adults, particularly when examining middle-aged and older adults together. Comparing means of test performance neglects intra-individual changes and better performances by middle-aged adults underestimate deteriorations in older populations by averaging effects. Consequently various statistical methods to assess intra-individual changes have been used to determine whether POCD has occurred. Methods include the '20% decline on 20% of the tasks', 'one standard deviation decline on two or more tasks', or the ISPOCD group's modified reliable change index (I-RCI), which have been discussed and examined in more depth by Lewis et al. (2006). Following their examination of the three statistical methods they conculded that using the modified reliable change index is preferred as it demonstrates the greatest combination of sensitivity and specificity in comparison to the other methods.

Statements of consensus were published [Murkin et al. 1995; Murkin et al. 1997] to guide researchers in choosing optimal assessments, reduce potential confounding factors to neuropsychological test performance, and appropriate analyses. Subsequent publications by the ISPOCD group [Rasmussen et al. 2001] have added to these recommendations. These include using the ISPOCD neuropsychological test battery, enrolment of a normative control group to control for practice effects and random variation, and analyses examining intra-individual changes [Rasmussen

et al. 2001]. The test battery assesses a balanced number of cognitive domains comprising of four standardised and sensitive neuropsychological measures: the Visual Verbal Learning Test [Brand & Jolles, 1985], assessing delayed recall & retrieval; memory; the Concept shifting test [Reitan, 1958], assessing executive functioning and speed of processing; the Stroop colour word inference test [Bohnen et al. 1992], assessing selective attention, mental speed, and interference susceptibility; and the letter-digit coding test [Lezak, 1995], assessing processing & psychomotor speed. Seven parameters from the four tests are used to compare intra-individual changes between assessment sessions.

To date there has not been a systematic review of literature examining POCD in a non-cardiac surgical population using general anaesthesia. Given the risk for cognitive decline following surgery, the projected increase of older adults likely to attend and survive non-cardiac surgery, and the known vulnerability of older adults to cognitive dysfunction, it is important that clinicians are aware of POCD in the older adult population. This is particularly important when examining older adults presenting with cognitive complaints given the likelihood they may have had a recent surgical procedure. Therefore, our aim is to systematically review the incidence of, risk factors contributing to, and features associated with, POCD in an older adult non-cardiac surgical population undergoing general anaesthesia.

Method

Objective

This systematic review aimed to address the question: In the older adult non-cardiac surgical population undergoing general anaesthesia:

- What is the incidence of POCD?
- What risk factors contribute to POCD?

- What are the features of POCD?

Search Strategy

A number of sources were used to identify studies for possible inclusion in this review. These included a search across the following electronic bibliographic databases:

All EBM Reviews CDSR, ACP Journal Club, DARE, CCTR

CINAHL (1982-2006)

EMBASE (1980-2006)

Medline (1966-2006)

PsychInfo (1985-2006)

Search Terms

The electronic search used eight key terms to reflect the main components of the systematic review question. The following terms were used in the search of the electronic databases

1. Postoperative cognitive dysfunction
2. POCD
3. cognitive impairment
4. neuropsychological outcome
5. cognitive deficit
6. postoperative outcome
7. surgery
8. anaesthesia
9. 1-2 combined using OR

10. 3-5 combined using OR
11. 6-8 combined using OR
12. 10-11 combined using AND
13. 9 & 12 combined using OR

Duplicates were removed and searches limited to English Language and publication year 1993-2006. Citation lists of retrieved studies were examined and hand searches of key journals, British Journal of Anaesthesia, Acta Anaesthesiologica Scandinavica, and Anaesthesia, were carried out to identify further articles. Reference lists were also reviewed from retrieved articles.

Inclusion Criteria

- Non-cardiac or non-neurological surgery using general anaesthetic.
- Participants aged ≥60 years.
- Standardised and reliable neuropsychological assessments used to assess cognitive functioning (not just cognitive screen).
- Studies assessing intra-individual preoperative and postoperative cognitive change.
- A normal control group recruited to control for practice effects on neuropsychological tests, normal ageing, and test variation.
- Sensitive method of statistical analysis used to ascertain cognitive decline.
- Measures of cognitive performance detailed as outcome measures.
- Peer reviewed journal article.

Results

Outcome of Search Process

The computerised search yielded 507 papers. Only 26 were retained as being relevant to the research question on the basis of their titles and abstracts. Of the 26 articles 18 did not meet inclusion criteria (see Appendix 2.2). No further papers were identified from searching the reference lists of papers included from the electronic search or from hand searches of key journals. A total of eight studies were reviewed.

Characteristics of Excluded Papers

Studies were excluded if they did not report separate incidences of POCD for older age groups. Therefore a total of 5 studies were excluded [Abildstrom et al. 2004; Ancelin et al. 2001; Grichnik et al. 1999; Linstedt et al. 2002; Moller et al. 1993]. Three studies were excluded due to using insensitive cognitive screening tools such as the MMSE [Chen et al. 2001; Milisen et al. 1998; Papaioannou, 2005]. Five were excluded because cognitive functioning was not formally assessed preoperatively [Bennett et al. 2004; Gruber-Baldini et al. 2003], postoperatively [Kaneko et al. 1997], or not at all [Rodig et al. 1999; Ward et al. 2005]. Two were excluded for not assessing acute postoperative functioning when assessing late outcome [Hall et al. 2005; Tamura et al. 2004]. Two studies were excluded for failing to recruit a normal control group or to control for learning or practice effects [Campbell et al. 1993; Williams-Russo et al. 1995]. One meta-analysis was excluded because it combined POCD incidences from general, regional, and local anaesthesic populations [Rasmussen, Siersma, and the ISPOCD group, 2004].

Assessment of Methodological Quality

The methodological quality of RCT and cohort studies was assessed using checklists adapted from the Scottish Intercollegiate Guidelines Network (SIGN) 'Guideline Developers Handbook' [Scottish

Intercollegiate Guidelines Network, 2004]. Criteria devised for assessing methodological quality also included factors recommended by the 'Statement of Consensus' and ISPOCD group [Murkin et al. 1995; Murkin et al. 1997; Rasmussen et al. 2001]. The checklists include criteria assessing the research aims, population, design, neuropsychological assessment battery used, confounding factors, and statistical analyses (see appendix 2.3).

All studies were scored on 44 factors of methodological quality. The reviewer was not blind to the author, institutions, journal of publication, or results. Possible scores ranged from 0 to 54, as higher weightings were given to important methodological items such as recruitment of an adequate control group, and were transferred into quality categories representing the overall percentage of quality criteria met:

A = $\geq$ 75% (high quality – all or most criteria have been fulfilled)

B = 60-74% (moderate quality – an adequate number of the criteria have been fulfilled)

C = 50-59% (low quality – some of the criteria have been fulfilled)

D = $\leq$ 49% (poor quality – very few of the criteria have been fulfilled).

No meta-analytic techniques were conducted in the present review given the heterogeneity of anaesthetic agents, time of preoperative and postoperative assessments, and surgical procedures used, in addition to certain methodological limitations of studies. Indeed, the methodological limitations highlighted within a recent systematic literature review of POCD in cardiac populations indicated that a discursive review would be more appropriate [Van Dijk et al. 2000].

Data Extraction

Data were extracted from each of the included studies. The data reflected the variables identified in the inclusion criteria and the aim of the review. A summary of the data extracted for each study is presented in Table 1.

[Insert Table 1. here]

Of the 8 studies reviewed,

4 met criteria for an A quality rating: Abildstrom et al. 2000
Canet et al. 2003
Moller et al. 1998
Rasmussen et al. 2003

4 met criteria for a B quality rating: Dijkstra et al. 1999
Rasmussen et al. 1999
Rentowl & Hanning, 2004
Rohan et al. 2005

No studies met criteria for a C or D quality rating, therefore the quality of papers' examined in the review are considered to be of moderate to high quality.

Reliability of Quality Rating

An independent examiner rated all studies included in this review and the index of agreement was 87% according to the category ratings (Cohen's Kappa co-efficient statistic= 0.874; excellent inter-rater agreement). Disagreement on one category was a result of a one-point difference causing a crossing of the category threshold of quality from B to A. The author and independent examiner met

to review disagreement on one factor of methodological assessment and agreed on score weighting following a short discussion.

Review of Findings

Studies will be reviewed in order of quality rating allocated within the subheadings: Incidence; Risk; Features.

Incidence

The reported incidences of POCD are shown in table 2.

[Insert Table 2. here]

20-24 Hours Postoperatively

Of eight studies included in this review only one investigated the incidence of POCD 20-24 hours postoperatively [**Rohan et al. 2005;** *moderate quality*] using a randomised design comparing two anaesthetic agents. The sample size of 30 and an age-matched control group (n=15) was supported by a power calculation. The ISPOCD RCI method was used to determine POCD [Moller et al. 1998], which has been shown to be reliable and sensitive [Lewis et al. 2006; Keizer et al. 2005]. Incidence of POCD at 20-24 hours following surgery was 47% (95% CI 21-72%) and was significantly greater than the incidence of 7% (95% CI 6-19%) within the control group (p=0.03). Nevertheless, the external validity was reduced as the sample is not considered to be entirely representative of the older adult population as exclusion criteria included pre-existing cognitive dysfunction. The method used to assess cognitive dysfunction further reduced validity as only two components of the ISPOCD test battery were administered thus cognitive domains examined were unbalanced. In addition, factors known to contribute to test performance variability were not

controlled for (e.g., testing environment, postoperative pain, acute testing of cognitive functioning 20-24 hours following anaesthetic agent). Therefore the incidence of cognitive dysfunction 20-24hours postoperatively is likely to be overestimated.

One week postoperatively

Six out of eight papers investigated the incidence of POCD at one week, or on day of discharge, following surgery [Moller et al. 1998 [*high quality*]; Canet et al. 2003 *[high quality*]; Rasmussen et al. 2003 *[high quality*]; Dijkstra et al. 1999 [*moderate quality*]; Rasmussen et al. 1999 [*moderate quality*]; and Rentowl & Hanning, 2004 [*moderate quality*].

Moller et al. [1998; *high quality*] examined POCD in 947 elderly patients aged 60-79 undergoing major surgery via a multi-centre prospective cohort design. A healthy non-surgical control group was recruited by newspaper advertisement using the same criteria as patients (n=176) to control for practice effects using the ISPOCD test battery. The sensitive I-RCI method to determine and define POCD was used. Moller et al. (1998) found that one week following surgery, or on day of discharge, the incidence of patients found to have POCD using general anaesthesia was 25.8% (95% CI 23.1-28.5) and was significantly greater than 3.4% (95% CI 1.3-7.3) within the control group ($p<0.0001$). Nevertheless, external validity was reduced due to sample bias (background data for refusals not being available i.e., refusal may be specific to vulnerable or at risk patients and exclusion criteria included pre-existing cognitive dysfunction) and not controlling for confounding variables that may have contributed to random variation (reduced environmental consistency between testing sessions and assessing patients one day preoperatively when anxiety is increased).

Rasmussen et al. [2003, *high quality*] investigated the effects of general anaesthesia (n=217) in comparison to regional anaesthesia (n=221) in a randomised controlled clinical trial using the sensitive ISPOCD method to determine and define POCD. Data to control for practice effects were those obtained during the Moller et al. (1998) study. Using an intention to treat analysis, one week following surgery the incidence of patients found to have POCD undergoing major surgery using general anaesthetic was 19.7% (95% CI 14.3-26.1) and was significantly greater than the incidence of 3.4% (95% CI 1.3-7.3) in controls. When using a per protocol analysis the incidence of POCD at one week was found to be 21.2% (95% CI 15.0-28.4) and was also significantly greater than the incidence found within controls. Nevertheless the external validity of the study is reduced due to a number of factors such as no prospective power calculation determining sample size and sample bias (as level of education was not controlled for, a factor known to be more vulnerable to POCD and exclusion criteria included pre-existing cognitive dysfunction). In addition, confounding variables known to affect performance (reduced environmental consistency between testing sessions and assessing patients one day preoperatively) were not adequately controlled.

Canet et al. [2003; *high quality*] investigated POCD in 372 patients undergoing various minor surgical procedures using general anaesthetic in a multi-centre prospective between groups cohort design. Patients were allocated to inpatient or outpatient care according to local practice rather than randomisation. The ISPOCD test battery was administered and the I-RCI methods to determine and define POCD using control data from Moller et al. (1998) were employed. At approximately one week postoperatively the incidence of patients found to have POCD undergoing minor surgery using general anaesthesia was 6.8% (95% CI 4.3-10.1), not significantly differing to the incidence of 3.4% (95% CI 1.3-7.3) found in controls. The higher incidence found in patients therefore may be a result of random variation. Cognitive dysfunction however significantly differed between inpatients and outpatients at one week (9.8% [95% CI 5.7-15.4] *vs.* 3.5% [95% CI 1.4-8.0]; p=0.033). However on

inspection of confidence intervals it is evident that control group values capture values for patients indicating 'no effect'. The external validity of the study is further reduced as it was not supported by a power calculation (therefore vulnerable to Type II error), demonstrated sampling bias (exclusion criteria included pre-existing cognitive dysfunction), and did not control for confounding variables that may contribute to random variation (reduced environmental consistency between testing sessions and assessing patients one day preoperatively).

Dijkstra et al. [1999; *moderate quality*] investigated POCD and cognitive complaints in 56 older patients following major non-cardiac surgery using a prospective cohort design. The ISPOCD test battery was administered to patients, and the I-RCI method was applied to determine and define POCD. Controls were recruited via newspaper advertisement using the same inclusion criteria for patients (n=50). One week following surgery the incidence of POCD was 27% (CI not stated), and was significantly greater than 6% (CI not stated) found in recruited controls (p=0.048). As confidence intervals are not provided range of effect sizes cannot be examined when interpreting differences between patients and controls. This is a major limitation as it is the effect size that determines the importance of findings, not the presence of statistical significance. Also, the sample size was not supported by a power calculation. The external validity of the study was significantly reduced as the control group is not considered to be a suitable comparison for patients as they were significantly younger and more educated than patients. Even after adjustment for these variables patients still performed significantly worse on 3 test variables preoperatively, therefore methods employed to control for learning effects may not be reliable. Sampling bias (exclusion criteria included pre-existing cognitive dysfunction) and not controlling for confounding variables (reduced environmental consistency between testing sessions and assessing patients one day preoperatively) further reduce external validity.

Rasmussen et al. [1999; *moderate quality*] examined diazepam and its relationship with POCD, one week postoperatively, or on day of discharge, in elderly patients. The sample was a subgroup of patients (n=35) within the Moller et al. (1998) study, therefore methods to identify and determine POCD were that of the ISPOCD group. One week following surgery the incidence of POCD in patients was 48.6% (95% CI 31.4-66.0), which was significantly greater than the 3.4% (95% CI 1.3-7.3) found in controls. However the external validity and methods to reduce bias within the study is significantly reduced as five patients had postoperative complications and confounding factors known to affect test performance were not controlled for in analyses (mood and postoperative benzodiazepine prescription less than 24 hour before the postoperative neuropsychological test). Therefore changes in test performance are significantly vulnerable to confounding factors and incidences are considered unreliable.

Rentowl & Hanning [2004; *moderate quality*] recruited 53 patients undergoing major surgery to pilot whether odour identification deficit could be a marker for POCD using a prospective cohort design. The ISPOCD test battery and I-RCI methods to determine and define POCD were employed using control data from Moller et al. (1998). Complete data were available for only 34 patients. At the first postoperative test session (7-15 days postoperatively) the incidence of POCD was 8.1% (95% CI 0.0-16.9) and did not differ significantly from controls (3.4%, 95% CI 1.3-7.3). Confidence intervals for effect sizes are wide indicating low power to detect an effect (vulnerable to Type II error), which is likely to have resulted from the sample size not being supported by a prospective power calculation. The external validity and methods to reduce bias within the study is also inadequate due to sampling basis (background data was not examined for patients who dropped out during the study therefore withdrawal may be specific to vulnerable or at risk patients) and not

controlling for confounding variables that may have contributed to random variation (reduced environmental consistency between testing sessions and assessing patients one day preoperatively).

The reliability of some incidences approximately one week postoperatively are questionable due to failure to control important confounding factors [Rasmussen et al. 1999], reporting non-significant results [Canet et al. 2003; Rentowl & Hanning, 2004] and failure to report effect sizes [Dijkstra, et al. 1999]. It can be reported however that the incidence of POCD approximately one week following major surgery in cognitively intact older adults ranges from 14.3% to 28.5%, at the 95% confidence interval [Moller et al. 1998 & Rasmussen et al. 2003; high quality].

Three months postoperatively

A number of studies did not find a significant difference between neuropsychological test performance in patients and controls three months postoperatively [Dijkstra et al. 1999; Canet et al. 2003; Rentowl & Hanning, 2004]. Confidence intervals reported for studies captured values reflecting no effect at the 95% confidence interval. Accordingly, these studies lacked statistical power and non-significant results may be an artifact of Type II error.

Moller et al. [1998] found the incidence of cognitive dysfunction at three months postoperatively to be 9.9% (95% CI 8.1-12.0) and was significantly greater than the incidence of 2.8% (95% CI 0.9-6.6) found in controls (p=0.0037). However, minor reduction of external validity is apparent due to having a partially unrepresentative sample and not controlling for some confounding factors.

Using an intention to treat analysis **Rasmussen et al.** [2003] found the incidence of cognitive dysfunction in patients to be 14.3% (95% CI 9.5-20.4), significantly greater than the incidence of 2.8% (95% CI 0.9-6.6) within controls at three months. When using a per protocol analysis the

incidence was also significantly greater than controls 13.1% (95% CI 8.1-19.7). External validity of results are reduced however due to lack of statistical power and sample bias.

No study reported whether POCD at three months was persisting from one week with exception from Rentowl & Hanning (2004) who found no patient with POCD at both test sessions. Patients defined as having POCD at three months therefore may have cognitive decline for other reasons if dysfunction was not identified postoperatively at one week. Therefore it is questionable if cognitive decline at three months can reliably be classified as POCD.

1-2 years postoperatively

One study examined POCD after a significant period following surgery. **Abildstrom et al.** [2000; *high quality*] investigated the persistence of POCD at 1-2 years by following-up 336 patients from the Moller et al. (1998) cohort. Patients were administered the ISPOCD test battery and POCD was determined using the I-RCI method. Control data were obtained from 47 of the original controls. At 1-2 years, 10.4% (95% CI 7.2-13.7) of patients were found to have cognitive dysfunction, a similar incidence to that found in controls (10.6%, 95% CI 1.7-19.4). This suggests that observed cognitive decline may have occurred due to normal ageing. However, of patients who had completed all testing sessions, only 3 (0.9%) had POCD at all sessions. The likelihood of this occurring is 1:64 000 (0.002%). This incidence however may be grossly underestimated due to initial sampling bias, inadequate control group size and inconsistent test administration (different examiner and inter-rater agreement not reported).

Risk Factors for Development of POCD

Risk factors found to be associated with the development of POCD are shown in table 3.

[Insert Table 3. here]

Moller et al. [1998; *high quality*] used a multiple logistic regression to investigate associations between potential risk factors and the development of POCD. A significant relationship between early POCD (at one week) and increasing age (odds ratio OR 1.3 [95% CI 1.0-1.7], p=0.03), increasing duration of anaesthesia - difference of 1 hour (OR 1.1 [95% CI 1.0-1.3] p=0.01), little education (OR 0.6 [95% CI 0.4-0.9], p=0.002), second operation (OR 2.7 [95% CI 1.1-6.6], p=0.03), postoperative infection (OR 1.7 [95% CI 1.0-2.8], p=0.04), respiratory conditions (OR 1.6 [95% CI 1.0-2.6], p=0.05) and centre (p=0.0001) was found. The authors report that effect of centre in the risk-factor analysis for early POCD may reflect differences in procedures, anaesthetic agents, and population characteristics, but cannot be explained by the analysis. Significant associations were found between POCD at three months and age (OR 2.1 [95% CI 1.4-2.9], p<0.0001) and benzodiazepines before surgery (i.e., protective) (OR 0.4 [95% CI 0.2-1.0], p=0.03).

Despite finding no significant differences between patients and controls, **Canet et al.** [2003; high quality] used multiple logistic regression analysis to examine risk factors for POCD. They found associations with age greater than 70 (OR 3.8 [95% CI 1.45-10.1], p=0.01) and inpatient surgery (compared to outpatient; OR 2.8 [95% CI 1.05-7.4], p=0.04) for POCD at one week. The validity of relationships is questionable however given the absence of POCD being reliably identified within the patient group initially due to Type II error.

Dijkstra et al. [1999; *moderate quality*] investigated potential risk factors contributing to intra-individual changes using a stepwise hierarchical multiple regression model. Factors included in the analysis did not contribute significantly to the total explained variance in dependant variables (short

and long term intra-individual changes). However this may be a result of having an inadequate control group or reduced power for statistical analysis resulting in Type II error.

Rasmussen et al. [1999; *moderate quality*] found that blood concentrations of diazepam and desmethyldiazepam in patients with and without POCD did not differ significantly (Mann-Whitney test, $p>0.4$). In a multiple linear regression analysis only age was found to predict intra-individual change at one week. The analysis was repeated excluding patients who had received zopiclone 24 hour before testing however no further predictors were identified.

Rentowl & Hanning [2004; *moderate quality*] used binary logistic regression analysis to investigate associations between POCD and potential risk factors. No associations between odour identification, age, smoking, alcohol intake, gender or MMSE score and POCD at one week or three months were found. This may also be an artifact of Type II error and not entering, or controlling for, factors known to contribute to the development of POCD [Moller et al. 1998].

Abildstrom et al. [2000; *high quality*] used multiple logistic regression analysis to investigate risk factors for persisting POCD at 1-2 years following surgery. Significant risk factors identified were age (OR 2.58 [95% CI 1.42-4.70], $p=0.02$), early POCD one week (OR 2.84 [95% CI 1.35-5.96], $p=0.006$), and infection within the first 3 postoperative months (OR 2.61 [95% CI 1.02-6.68], $p=0.045$).

Four out of five studies did not investigate whether early POCD (at approximately one week) was a significant risk factor for POCD at three months [Moller et al. 1998; Canet et al. 2003; Rasmussen et al. 2003; Dijkstra et al. 1999]. This would seem important given that the prevalence of persisting POCD is not clear from initial analyses; therefore this is a limitation of the current literature.

Features of POCD

Features or patterns of cognitive deterioration were not reported for any study apart from Dijkstra et al. (1999). This may be a result of most studies using z-score transformations between individual test scores to calculate POCD, whereby encompassing general deterioration and substantial decline in two or more areas of cognitive functioning [Moller et al. 1998; Abildstrom et al. 2000; Rasmussen et al. 2003; Canet et al. 2003; the ISPOCD groups).

Features of POCD found within the Dijkstra et al. (1999) sample encompassed deterioration of sensorimotor speed, memory, processing speed of general information and interference susceptibility at one week following surgery. Unfortunately however methodological limitations such as lack of power and an inadequate control group reduces the external validity of findings and therefore cannot be generalised.

Discussion

Overall, the present review provides substantial support that relatively healthy older adults, with no pre-existing cognitive difficulties, who undergo general anaesthetic for major non-cardiac surgery are at risk for post-operative cognitive dysfunction at one week and three months post-surgically. At 1-2 years, persisting POCD was found in <1% [Abildstrom et al. 2000] of patients suggesting the prognosis for an elderly patient with early POCD is good. Methods to determine and define POCD are extremely sensitive and reliable if sample sizes are adequately powered to reduce Type II error rate. Thus it is recommended that clinicians should consider an acute onset of cognitive decline, supported by reduced performance on neuropsychological tests as resulting from POCD if patients have major surgery within three months of presentation.

However, studies included in this review were considered to have non-representative samples of the older adult or general surgical population as they exclude patients with pre-existing cognitive, psychiatric or central nervous system disorders, as well as patients taking tranquillisers or anti-depressants. Studies have been criticised for this selection bias [Dijkstra & Jolles, 2002], as patients meeting these criteria have to attend for surgical procedures as frequently as other individuals. There is also evidence that pre-existing deficits predict postoperative cognitive dysfunction or exacerbate cognitive decline [Bergren et al. 1987; Chung et al. 1989; Millar et al. 2001; Smith et al. 1986], thus the true incidence of POCD may be grossly underestimated. It was also observed that the assessment of POCD did not adhere entirely to the Statement of Consensus Guidelines [Murkin et al. 1995; 1997] by using inconsistent testing environments and assessing patients one day prior to surgery.

Researchers have therefore asked 'is POCD a clinical condition or just variability in test performance given the lack of consistency and correlation between test results and subjective cognitive complaints' [Rasmussen et al. 2001]. To investigate this question the ISPOCD group conducted a meta-analysis of four ISPOCD studies (patients n=2536; controls n=359) to examine if variability in neuropsychological testing could affect the interpretation of POCD [Rasmussen et al. 2004]. They found that test variability contributed to low consistency between postoperative test sessions therefore the incidence of POCD at one week following minor surgery may be due to random variation as previously considered, but it did not explain the detection of cognitive dysfunction after major surgery.

Surprisingly, no study stated whether POCD at three months was persisting from one week. This raises questions surrounding the appropriateness of defining POCD in patients who have reduced neuropsychological test scores at three months when they did not meet criteria for POCD at one week, particularly when confounding factors to test performance are likely to be prevalent at one week (e.g., pain, hospitalisation, anxiety). It would be difficult to attribute cognitive decline to surgical procedures at three months if decline is not evident earlier. Psychological factors such as mood, adjustment to a major life experience, or inactivity due to physical recovery may be factors contributing to poorer performance on neuropsychological tests, but these have not been examined in relation to cognitive functioning. Indeed, the absence of medical risk factors associated with POCD at three months may support this hypothesis particularly as mood was not entered into regression analyses although considered in the design by four studies.

In support, some authors proposed that other factors, not controlled for in study design, may have contributed to POCD. For example, Canet et al. (2003) suggest the hospital environment induces sleep deprivation, immobility, dehydration, and sensory overloading (as POCD was greater at one week in the inpatient group compared to outpatients) and Rohan et al. (2005) suggested stress responses to surgery, anxiety, and prolonged starvation within the first 24hours, may induce POCD. Unfortunately no study has yet examined the effects of psychological factors on the development of POCD, particularly as psychological factors may be reduced by psychological intervention thus the reduction of POCD may be viable. Nevertheless, despite mechanisms contributing to POCD (neurological dysfunction, motivation, mood, pain etc) remaining unclear because factors such as pain, motivation, mood, or fasting, were not controlled for, incidences remain a true reflection of POCD. Evidently, older adults are at risk of cognitive decline postoperatively and this may negatively impact on their recovery and quality of life.

Implications for Future Research

This review highlighted a number of important areas requiring further examination. For example it would be useful to examine the proportion of POCD at three months persisting from one week and to examine the contribution of psychological factors such as mood, anxiety, and stress-response (to the hospital environment) to POCD or test variation.

The recent literature has primarily been concerned with the reliability of identifying and determining POCD. Now that the literature has resolved many of its methodological difficulties it is reasonable to consider whether statistical differences between groups are also clinically significant [Rasmussen et al. 2001]. It is difficult to translate performances on neuropsychological test to functional abilities

outwith the hospital environment however original examination of POCD arose from concerns that cognitive impairment resulted from surgery and its effect on quality of life and independence. It seems that issues such as psychological or social effects of POCD have been neglected. It is recommended that these issues should be considered in future research.

It is widely accepted that when assessing neuropsychological functioning using standardised assessment measures that it is necessary to reduce confounding factors as those identified by exclusion criteria. However, this results in samples not being entirely representative of the older adult population. Therefore examination of the effects of surgery upon cognitive ability in patients with pre-existing cognitive, psychiatric or central nervous system disorders, is considered paramount to add to the current literature to represent the whole older adult population.

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Table 1. Summary table of sample characteristics, assessment period/battery, method of defining POCD, and study findings.

Study Author/Year/Title	Quality Rating	Surgical Sample(s)	Assessment Time period(s) & Battery used	Method of defining POCD	Incidence, Risk Factors, & Features
Albistrom, Rasmussen, Rentowl, Hanning, Rasmussen, Kristensen, Moller, the ISPOCD group, 2000. Cognitive Dysfunction 1-2 years after non-cardiac surgery in the elderly. (Follow-up study of Moller et al 1998)	A	1. n = 336 2. Major abdominal; non-cardiac thoracic; or orthopaedic. 3. General Anaesthetic 4. Median = 69; Range 60-86. Age 60-69 = 183, Age 70 above = 153 5. females: males = not stated. Control Sample 1. n = 47 2. Non-hospitalised volunteers. 3. n/a 4. Median = 71; range 60-83. females : male = 30; 64% Power Original study initial calculation n= 900.	1. one day preoperatively 2. discharge or day 7 postoperatively at latest. 3. 3 months postoperatively **4. 1-2 years postoperatively** **ISPOCD Battery** 1. Visual Verbal learning Test (cumulative number of words recalled in three trials and the number of words). 2. Concept Shifting Test (time and number of errors in part C) 3. Stroop Colour Word Inference Test (time and number of errors in part 3) 4. 4.Letter-Digit Coding Test (number of correct answers)	ISPOCD RCI method	**Incidence** of persisting POCD from 1 week at 1-2 years = <1% Cognitive dysfunction at 1-2 years= 10.4% (95% CI 6.9-13.5%) **Risk Factors** = Age (p=0.02; Odds ratio 2.58 [1.42-4.70]), early POCD (p=0.006; Odds Ratio 2.84 [1.35-5.96]), and infection within the first three postoperative months (p=0.045; Odds Ratio 2.61 [1.02-6.68] were found to be predictors of long-term dysfunction. No significant relationship between POCD at 3 months and 1-2 years (p=0.97). Duration of anaesthesia, respiratory complications, education, cancer & benzodiazepines before surgery not risk factors for late POCD. **Features** = Not stated. Comments Control Group – incidence of cognitive decline = 10.6%. **Conclusions** POCD is a reversible condition in majority of elderly patients after general surgery, but may persist in approx 1%. Prognosis of an elderly patient with early POCD is good as majority appear to recover.
Canet, Raeder, Rassmussan, Enlund, Kuipers, Hanning, Jolles, Korttila, Siersma, Dodds, Abilstrom, Sneyd, Vila, Johnston, Munoz Corsini, Silverstein, Nielsen, & Moller, for the ISPOCD2 investigators, 2003. POCD following Minor Surgery.	A	1. n= 372 (in-patient n=199; out-patient n =173). 2. Minor surgery. 3. General Anaesthesia; in vs outpatient. 4. Median age inpatient = 67.8, range 60.8-80.2; Median age outpatient = 67.6, range 61.2-79.9. 5. Female : Male inpatient = 113, 57%; Female : Male outpatient = 85, 49%. Control Sample 1. n = 176 2. Non-hospitalised UK volunteers from ISPOCD1 control group. 3. n/a 4. Median = 67; range 61-81. 5. females : male = 75; 43% Power N=600 (300 in- and 300 outpatients) allow a detection of a decline in POCD of between 25% in one group (previous study) to 15% in the other group with a power of 0.90 at the significance level of 0.05.	1. one day preoperatively 2. approx 7 days postoperatively 3. 3 months postoperatively. **ISPOCD Battery** 1. Visual Verbal learning Test (cumulative number of words recalled in three trials and the number of words). 2. Concept Shifting Test (time and number of errors in part C) 3. Stroop Colour Word Inference Test (time and number of errors in part 3) 4. Letter-Digit Coding Test (number of correct answers)	ISPOCD RCI method	**Incidence** of POCD at 1week = 6.8%(95% CI 4.3-10.1) Cognitive dysfunction at 3 months = 6.6% (95% CI 4.1-10.0) **Risk Factors** = (at 1 week) age greater than 70 (p=0.01) and inpatient surgery (compared to outpatient; p=0.04). No risk factors found at 3 months. Overall, longer hospitalisation is a risk factor for POCD. **Features** = Not stated. Comments Control Group – incidence of cognitive decline 1 week = 3.4% (95% CI 1.3-7.3). Control Group – incidence of cognitive decline 3 months = 2.8% (95% CI 0.9-6.5). **Conclusions** Incidence of POCD at 1 week was significantly lower in elderly patients undergoing minor surgery than major surgery (p=0.001 and p=0.08, respectively). Lower incidence of POCD found in day-case setting than in patients hospitalised for 1 night. Factors most likely to explain development of POCD are age, hospitalisation, extension, and duration of surgery.

Table 1. continued

Study Author/Year/Title	Quality Rating	Surgical Sample(s)	Assessment Time period(s) & Battery used	Method of defining POCD	Incidence, Risk Factors, & Features
Moller, Cluitmans, Rasmussen, Houx, Rasmussen, Canet, Rabbitt, Jolles, Larsen, Hanning, O'Langeron, Johnston, Lauven, Kritsensen, Biedler, van Beem, Fraidakis, Silverstein, Beneken, Gravenstein, for the ISPOCD group, 1998. Long term POCD in the elderly: ISPOCD1 study	A	1. n = 947 2. Major abdominal; non-cardiac thoracic; or orthopaedic. 3. General Anaesthetic 4. Median = 68; Range 60-79. 5. females: males = 464, 49%. Control Sample 1. n = 176 2. UK Non-hospitalised volunteers. 3. n/a 4. Median = 67; range 61-81. 5. females : male = 75; 43% Power Assumed an overall risk of long-term cognitive dysfunction of 10% and the association was quantified as an odds ratio of 1.5 for patients with hypoxaemia 1 SD below the mean. A sample size of n=900 allowed for risk factors to enter the model with a multiple correlation coefficient to hypoxaemia of up to 0.3.	1. preoperatively 'generally day before surgery' 2. discharge or day 7 postoperatively 3. 3 months postoperatively **ISPOCD Battery** 1. Visual Verbal learning Test (cumulative number of words recalled in three trials and the number of words). 2. Concept Shifting Test (time and number of errors in part C) 3. Stroop Colour Word Inference Test (time and number of errors in part 3) 4. Letter-Digit Coding Test (number of correct answers)	ISPOCD RCI method	**Incidence** of POCD at 1week = 25.8% (95% CI 23.1-28.5) Cognitive dysfunction at 3 months = 9.9% (95% CI 8.1-12.0) **Risk Factors** = significant relation between early postoperative cognitive dysfunction, and increasing age (p=0.03), increasing duration of anaesthesia (p=0.01), little education (p=0.002), second operation (p=0.03), postoperative infection (p=0.04), and respiratory conditions (p=0.05). Significant associations between long-term (3 months) POCD and age (p<0.0001; odds ratio 2.1 [1.4-2.9]) and benzodiazepine before surgery (protective; p=0.03; odds ratio 0.2-1.0]). **Features** = Not stated. Comments Control Group – incidence of POCD 1 week = 3.4% (95% CI 1.3-7.3); 3 months = 2.8% (95% CI 0.9-6.5). Conclusions Anaesthesia and surgery cause long-term POC decline in the elderly and risk increases with age. Neither hypoxaemia nor hypotension related to risk. Whether POCD is a permanent disorder of irreversible brain damage associated with structural cerebral changes and neuron loss still need to be confirmed.
Rasmussen, Johnston, Kuipers, Kristensen, Siersma, Jolles, Papaioannou, Abildstrom et al ISPOCD2 Investigators, 2003. Randomised Controlled Clinical Trial: General vs Regional Anaesthesia.	A	1. n= 428 (GA=217) 2. non-cardiac surgery (hip/knee replacement; gynaecology; vascular, urology; gastrointestinal). 3. General Anaesthesia (GA) vs. Regional Anaesthesia (RA) 4. Mean age (GA) = 70.8 range 61.3-84.1) 5. Female : Male = 136, 63%. Control Sample 1. n = 176 2. UK Non-hospitalised volunteers. 3. n/a 4. Median = 67; range 61-81. 5. females : male = 75; 43% Power N= 1400 would detect a difference in POCD after 3 months between 5% after regional anaesthesia and 10% after general anaesthesia with a power of 0.90 at the 0.05 significance level.	1. one day preoperatively 2. 7 days postoperatively 3. 3 months postoperatively **ISPOCD Battery** 1. Visual Verbal learning Test (cumulative number of words recalled in three trials and the number of words). 2. Concept Shifting Test (time and number of errors in part C) 3. Stroop Colour Word Inference Test (time and number of errors in part 3) 4. Letter-Digit Coding Test (number of correct answers).	ISPOCD RCI method	**Incidence** of POCD at 1week = 19.7% (95% CI 14.3-26.1%). Cognitive Dysfunction at 3 months = 14.3% (95% CI 9.5-20.4%). **Risk** = No effect for RA vs. GA using intention to treat approach. Significant difference between groups at one week using a per protocol analysis (p=0.04). Results suggest negative effect of the GA agents or postoperative analgesic regimen at 1 week on cognitive functioning. Features = Not stated Comments Regional Anaesthesia Group – incidence of cognitive decline 1 week= 12.5% (95% CI 8.0-18.3%); 3 months= 13.9% (95% CI 9.0-20.2). Conclusions No significant difference in the incidence of cognitive dysfunction 3 months after either general or regional anaesthesia. No evidence to suggest a causative relationship between general anaesthesia and long-term POCD.

Table 1. continued

Study Author/Year/Title	Quality Rating	Surgical Sample(s)	Assessment Time period(s) & Battery used	Method of defining POCD	Incidence, Risk Factors, & Features
Dijikstra, Houx & Jolles, 1999. Cognition after major surgery in the elderly: test performance and complaints.	B	1. n = 48 2. Major abdominal, thoracic, non-cardiac or orthopaedic surgery. 3. General Anaesthetic. 4. Mean = 68.2; Range 60-85. 5. females: males = 35; 73%. Control Sample 1. n = 50 2. Healthy volunteers recruited from newspaper. 3. n/a 4. Mean = 64.5; range 57-78. 5. females : male = 23, 46% Power Not stated.	1. one day preoperatively **2.** 7 days postoperatively **3.** 3 months postoperatively **ISPOCD Battery** 1. Visual Verbal Learning Test 2. Selective attention using the Stroop colour-word test 3. Concept shifting test 4. Letter-digit substitution test	ISPOCD RCI method	**Incidence** of POCD at 1 week = 27%. Cognitive Dysfunction at 3 months = 8%. Risk Factors = decreased performance on speed-related tasks one week following surgery. Age, years of education, sex, change on depression scale, duration of anaesthesia and days spent in hospital did not predict short or long-term change in cognitive performance. Poorer performance on the concept shifting task at 3 months correlated with Zung scale indicating poorer performance with higher Zung scores ($p<0.01$; $R^2=0.177$). After 3 months patients and controls showed improved performance compared to baseline. **Features** = Short-term dysfunction; sensorimotor speed, memory, processing of general information, and interference susceptibility. Comments Incidence of POCD differed significantly from controls at 1 week (6%; p=0.048) but not 3 months (2%; ns). **Conclusions** Cognitive dysfunction occurred in the elderly shortly after operation but not in the long term however a subgroup of patients (29%) suffer long-term self-reported cognitive complaints at 6 months and 8 (17%) of these still suffered from cognitive dysfunction.
Rasmussen, Steentoft, Rasmussen, Kristensen, Moller & the ISPOCD1 group, 1999. Benzodiazepines and postoperative cognitive dysfunction in the elderly.	B	1. n = 35 2. Major abdominal surgery. 3. General Anaesthetic, (subset of ISPOCD patients) 4. Mean = 68; Range 60-84. 5. females: males = 11; 31%. Control Sample (Moller et al, 1998) 1. n = 176 2. Healthy controls. 3. n/a 4. Mean = 67; range 61-81. 5. females : male = 75, 43% Power Based on a pilot study with benzodiaxepine concentrations and a power of 80%, Found that a group of 30 participants would detect a difference in neuropsychological test results corresponding to 1 SD between patients with benzodiazepine concentrations greater than or less than 0.1 μmol kg^{-1}.	1. one day preoperatively **2.** discharge or day 7 postoperatively **ISPOCD Battery** 1. Visual Verbal Learning Test 2. Selective attention using the Stroop colour-word test 3. Concept shifting test 4. Letter-digit substitution test	ISPOCD RCI method	**Incidence** of POCD at 1 week = 48.6% (95% CI 31.4-66%). **Risk** Factors = duration of anaesthesia and blood concentrations of diazepam & desmethyldiazepam did not correlate with the composite Z-score. Age correlated with composite Z-score (p=0.0046; regression coefficient 0.124yr^{-1}). **Features** = not stated. **Conclusions** No significant relationship was found between blood concentrations of benzodiazepines and change in cognitive function, 1 week after surgery. POCD 1 week after surgery in elderly patients could not be explained by concentrations of benzodiazepine at time of neuropsychological testing.

Table 1. continued

Study Author/Year/Title	Quality Rating	Surgical Sample(s)	Assessment Time period(s) & Battery used	Method of defining POCD	Incidence, Risk Factors, & Features
Rentowl & Hanning, 2004 Odour identification as a marker for POCD: A pilot study.	B	1. n = 53 2. major abdominal, orthopaedic or non-cardiac thoracic surgery. 3. General Anaesthetic. 4. Mean = 71; SD=6. 5. females: males = 28; 53%. Control Sample (Moller et al, 1998) 1. n = 176 2. Healthy controls. 3. n/a 4. Mean = 69; range 61-81. 5. females : male = 75, 43% Power Estimated from the ISPOCD study that approximately 25% of patients at 1 week and 10% at 3 months after would fulfil criteria for POCD. As it was a pilot study no power calculations were done. Instead they aimed to recruit the maximum number of patients possible with the resources available, which was estimated at 50.	1. preoperative - not stated 2. 7 days postoperatively 3. 3 months postoperatively **ISPOCD Battery** 1. Visual Verbal learning Test (cumulative number of words recalled in three trials and the number of words). 2. Concept Shifting Test (time and number of errors in part C) 3. Stroop Colour Word Inference Test (time and number of errors in part 3) 4. Letter-Digit Coding Test (number of correct answers)	ISPOCD RCI method	**Incidence** of POCD at 1 week = 8.1% (95% CI 0-16.9). Cognitive Dysfunction at 3 months = 11.8% (95% CI 0.9%-22.6%). **Risk Factors** = No association between odour identification and POCD at 1 week (p=0.257) or 3 months (p=0.144). No association found for Apoe E4 and POCD at 1 week and 3 months. No association between age, smoking, alcohol intake, gender of MMSE score and POCD at 1 week (p=0.432) and 3 months (p=1.0). **Features** = not stated. **Conclusions** Odour identification deficit was not associated with POCD.
Rohan, Buggy, Crowley, Ling, Gallagher, Regan & Moriarty, 2005. Increased incidence of POCD 24hr after minor surgery in the elderly.	B	1. n = 30 2. Minor urological or gynaecological. 3. General Anaesthetic; sevoflurane vs. propofol. 4. Median = 74.9; Range 67-86. 5. females: males = 7; 23%. Control Sample 1. n = 15 2. Hospitalised volunteers not undergone surgery in 12 months. 3. n/a 4. Median = 71; range 60-83. 5. females : male = 4; 27% Power Taking approx 5% as the incidence of POCD in control patients from previous studies at one week it was estimated that n=15 patients in each study group would be needed to show a difference in POCD between 45% and 5% assuming a type 1 error of 0.05 and a type II error of 0.2.	1. preoperatively, not stated. 2. 20-24hour after anaesthesia. 1. Visual Verbal learning test (cumulative number of words recalled in 5 trials plus the number of words at delayed recall). 2. Stroop Colour Word Inference Test (error scores from the second part of test)	ISPOCD RCI method	Incidence of POCD at 1day = 47% (95% CI 21-72%) in both anaesthesia groups. Risk Factors = n/a – no differences between anaesthesia type. Features = n/a. Comments Control Group – incidence of cognitive decline = 7% (95% CI 6-19%), significantly different p=0.03. Conclusions Incidence of POCD found in elderly patients 24hour following minor surgery using GA is higher than controls but no differences between anaesthetic techniques. Does not imply anaesthesia per se causes POCD rather that the perioperative experience induces POCD early in the postoperative period. No difference in s-100B protein or NSE between pre & post operative period therefore these markers are not influenced by anaesthesia.

Table 2. Incidence of POCD per time period

Paper	20-24 hour (95% CI)	% 1 week (95% CI)	% 3 months (95% CI)	% 1-2 years (95% CI)
Albistrom et al (2000)	-	24.8 (20.1-29.5)	10.3 (6.9-13.5)‡	<1% (CI not stated)†
Moller et al (1998)	-	25.8 (23.1-28.5)	9.9 (8.1-12.0) ‡	-
Canet et al (2003)	-	6.8 (4.3-10.1)	6.6 (4.1-10.0) ‡	-
Rasmussen et al (2003)	-	19.7 (14.3-26.1)	14.3 (9.5-20.4)‡	-
Dijkstra et al (1999)	-	27 (nr)	8 (nr)	-
Rasmussen et al (1999)	-	48.6 (31.4-66.0)	-	-
Rentowl & Hanning (2004)		8.1 (0.0-16.9)	11.8 (0.9-22.6)‡‡	
Rohan et al (2005)	47 (21-72)	-	-	-

† Persisting POCD from 1 week & 3 months
‡ Not stated if persisting POCD or new cases
‡‡Not persisting in any case
nr = not reported

Table 3. Risk factor associated with development of POCD

Period	Author/Year	Risk Factor found contributing to POCD	Significance	Odds Ratio	Confidence	Variance
1 week	Canet et al (2003)	Age greater than 70	0.01	3.8	1.45-10.1	-
		Inpatient surgery compared to outpatient	0.04	2.8	1.05-7.4	-
	Moller et al (1998)	Increasing age	0.03	1.3	1.0-1.7	-
		Centre	0.0001	ns	ns	-
		Increasing duration of anaesthesia	0.01	1.1	1.0-1.3	-
		Little education	0.002	0.6	0.4-0.9	-
		Second operation	0.03	2.7	1.1-6.5	-
		Postoperative infections	0.04	1.7	1.0-2.8	-
		Respiratory complications	0.05	1.6	1.0-2.6	-
	Rasmussen et al (1999)	Age	0.0046	-	-	R^2= 0.124yr^{-1}
3 months	Dijikstra et al (1999)	Concept shifting task performance poorer with higher depression scores	0.01	-	-	R^2=0.177
	Moller et al (1998)	Age	0.0001	2.1	1.4-2.9	-
		Benzodiazepines before surgery (protective)	0.03	0.4	0.2-1.0	-
1-2 years	Albistrom et al (2000)	POCD at 1 week	0.006	2.84	1.35-5.95	-
		Age (difference of ten years)	0.002	2.58	1.42-4.70	-
		Infectious complication up to 3 months postoperatively	0.045	2.61	1.02-6.68	-

ns = not stated

Chapter 3: Major Research Project Proposal

Psychological distress in disease-free breast cancer survivors completing tamoxifen therapy: the contribution of illness and treatment representations to psychological morbidity.

Prepared in accordance with guidelines in the Doctorate in Clinical Psychology Research Training Folder (see Appendix 3.1)

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SUMMARY OF PROJECT

Research has predominately examined patient psychological distress and morbidity during and following screening, diagnosis, early treatment, mastectomy, chemotherapy and radiotherapy in breast cancer patients. However, psychological morbidity or distress has not been examined in patients coming to the end of tamoxifen therapy, a significant marker in a women's recovery from breast cancer. Anecdotal evidence suggests breast cancer surgeons observe patients to be relieved at its discontinuance due to adverse side effects. However, patients have also been observed to be extremely anxious when about to complete a 5-year prescription of tamoxifen due to fears of cancer recurrence. The current study will examine the variation of distress related to tamoxifen therapy completion in a cohort of disease-free breast cancer survivors and explore potential relationships between treatment representations, illness perceptions, coping style, fear of recurrence, and personality, to variations of distress.

If the study is successful in identifying psychological characteristics predicting vulnerability for psychological distress prior to completing tamoxifen therapy, clinical psychologists in consultation with clinical staff can assist and educate relevant health professionals in the routine assessment and monitoring of patients to identify those at risk. Clinical psychology could therefore promote the psychosocial care of disease-free survivors through consultation and direct intervention, encouraging future early interventions to reduce tamoxifen related distress before impacting detrimentally on quality of life.

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INTRODUCTION

Breast cancer is the most common incident cancer among women in Scotland and accounts for 25% of the female cancer burden excluding non-melanoma skin cancer (National Health Service in Scotland, 1998). Being diagnosed at an earlier stage and the use of systemic adjunctive therapies such as chemotherapy and hormonal treatments has improved the likelihood of long-term, disease-free survivorship (Ganz et al., 2002; Wingo et al., 1999; Greenlee et al., 2000). Evidently, survival from breast cancer has improved over the last 20 years in Scotland, with 56% five year relative survival having been reported for those diagnosed between 1968 and 1972 (Black et al., 1993), compared to 70% for those diagnosed between 1988 and 1992 (Harris et al, 1998).

Despite increasing numbers of patients surviving breast cancer, research investigating psychological morbidity has typically examined factors impacting on adjustment to the diagnosis or treatment (mastectomy, lumpectomy, radiotherapy, or chemotherapy) of breast cancer. During the last decade however there has been an increase, albeit small, in research examining breast cancer survivorship and the long-term effects on quality of life outcomes, ranging from 1-10 years follow-up (Bower et al., 2000; Dorval et al., 1998; Ganz et al., 1996; Ganz et al., 1998; Ganz et al., 2002).

Adjunctive Hormonal Therapy

Many breast cancer patients who have undergone a surgical procedures, chemotherapy, or radiotherapy are prescribed adjunctive hormone therapy i.e., tamoxifen. Five years of tamoxifen therapy has been found to reduce the risk of breast cancer recurrences by 50%, and breast mortality by 28%, in women with early stage breast cancer who are estrogen receptor (ER)-positive (Early Breast Cancer Trialists' Collaborative Group, 1998). Although tamoxifen is alleged to reduce the incidence of coronary heart disease (Henderson et al., 1988) and osteoporosis (Turken et al., 1989),

these additional benefits are outweighed by the knowledge of serious side effects, such as the increase in incidence of uterine and liver cancers, thromboembolic disease and retinopathy (Fugh-Berman & Epstein, 1992), and deterioration in memory when combined with chemotherapy (Bender et al., 2005). Due to the negative outcomes associated with long-term administration, women are advised that tamoxifen will be prescribed for a maximum of five years. The end of tamoxifen therapy may be viewed as a transition from an 'acute' to 'extended' stage of survival whereby the patient has finally completed treatment and may have 'watchful waiting' for recurrence or experience great anxiety with the diminished contact with the health care team (Mullen, 1985).

Anecdotal evidence suggests that breast cancer surgeons and clinical psychologists have observed many patients being relieved or glad to finish tamoxifen therapy due to adverse side-effects associated with the drug, such as hot flushes and vaginal discharge, whereas other patients are observed to be extremely anxious, worrying that when they stop taking tamoxifen breast cancer will recur. Breast cancer survivors, who were disease-free for a minimum of two-years, and diagnosed at an earlier stage, were found to significantly believe in the role of tamoxifen in preventing the recurrence of their cancer (Stewart et al., 2001). No study to date has formally examined patient cognitions or emotions in relation to completing tamoxifen therapy as research has primarily focused on the drug's effectiveness, side effects, & factors contributing to adherence or early discontinuance. Psychosocially, no evidence of tamoxifen-related side effects have been found on mood, psychosocial or sexual functioning in women at high risk of breast cancer (Fallowfield et al., 2001). However in a sample of disease-free breast cancer survivors 5-10 years following primary treatment, those treated with chemotherapy, tamoxifen, or both together, were found to be associated with poorer functioning on several dimensions of quality of life compared to those who did not receive adjunctive therapy (Ganz et al., 2002).

The psychosocial impact of changing medication regimes in other clinical populations has also been neglected with the primary interest being the examination of psychological factors contributing to medication adherence. Goodacre & Goodacre (2004) found that rheumatoid arthritic patients whose disease-modifying anti-rheumatic drugs (DMARDs) were being discontinued, reported having increased anxiety, decreased expectations about their outcome, and concerns about running out of treatment options. This finding cannot be generalised to breast cancer survivors however given tamoxifen is prescribed for the prevention of a life-threatening disease recurring. Patients coming to the end of tamoxifen therapy have no control over its discontinuance, and other clinical populations are more likely to have other treatment choices.

Given the high number of women prescribed this risk reducing drug, and the significance of completing a 5-year prescription period whilst remaining disease-free, it would appear essential to examine psychological distress and factors that may contribute to individual variations of distress. This may assist health professionals identify breast cancer survivors who are more vulnerable to experience higher levels of distress than others. *'Failure to detect and treat elevated levels of distress jeopardises the outcomes of cancer therapies, decreases patients' quality of life, and increases health care costs. Psychosocial screening with prospective interventions is a necessary component of comprehensive cancer care'* (Zabora, et al., 2001; pp27).

Distress & Adjustment to Cancer

In the largest prevalence study of distress in cancer patients Zabora et al (2001) found that 32.8% of breast cancer patients met clinical caseness for distress and one group of researchers have classified breast cancer patients an 'at risk group' for distress compared to other oncology subgroups (Herschbach et al., 2004). Despite this, research also suggests that the majority of women with breast

cancer are well adjusted (Glanz et al., 1992; Omne-Ponten & Sjoden, 1994; Schover et al., 1995; Vickberg et al., 2000). Moderate to high levels of distress have been evident in the immediate aftermath of diagnosis and treatment in breast cancer patients (Fallowfield et al., 1990; Farragher, 1998; Kissane et al., 1998; Steginga et al., 1998). Varying degrees of distress have also been associated with different stages of breast cancer over a period of 3-5 years (Heim et al, 1997). Helgeson et al (2004) sought to identify distinct trajectories or patterns of mental and physical functioning over 4 years following breast cancer diagnosis and found the course of adjustment was not the same for all patients, with distinct patterns of change, mostly occurring within the first 13 months of diagnosis. Some women were found to steadily improve with time, whereas others showed marked deteriorations or improvements in functioning.

It is evident that factors other than clinical diagnosis and treatment choice contribute to individual variations in distress. Factors found to predict greater levels of distress in individuals in response to breast cancer diagnosis and early treatment have been a history of stressful life events (Butler et al., 1999), history of depression (Maunsell et al., 1992), personality (Millar et al., 2005), and fears of recurrence (Sneeuw et al., 1992; Mast, 1998, Moyer & Salvoy, 1998; Walker, 1997). Whereas factors associated with distress in women at risk for breast cancer include younger age (Lerman et al., 1994; Cull et al., 1999), optimism (Audrain et al., 1997), and coping style (Lerman et al., 1996; Audrain et al., 1997).

Adjustment to cancer can be defined as an ongoing process where the patient tries to manage emotional distress and gain control over ongoing cancer-related life events. Greer & Watson (1987) have identified 5 common adjustment styles to the diagnosis and treatment of cancer which include; fighting spirit, where the person sees the illness as a challenge and has a positive attitude to outcome;

avoidance or denial, where the person denies the impact of the disease, and threat from the diagnosis is minimised; fatalism, where diagnosis represents a minor threat with no control being exerted over the situation and consequences thought to be accepted with equanimity; helplessness and hopelessness, where the person is overwhelmed by the enormity of the threat of cancer and attention bias is on the impeding loss of life or on the illness as a defeat; and anxious preoccupation, where anxiety is the predominant affect filled with compulsive searching for reassurance (Moorey & Greer, 2002).

A patients adjustment style to breast cancer is therefore hypothesised as a contributing factor to the level of distress found in patients about to complete tamoxifen therapy. Specifically, it could be hypothesised that patients with adjustment styles such as fighting spirit, avoidance or denial, and fatalism, would experience lower levels of distress when tamoxifen therapy is discontinued compared to patients with adjustment styles such as helplessness & hopelessness and anxious preoccupation, as patients which the latter adjustment coping styles may be psychologically dependent on the risk reduction affects of tamoxifen in relation to cancer recurrence and become more distressed when approaching drug discontinuance.

Illness Representations

One theoretical model that has been successful in explaining or predicting psychological distress or morbidity in a variety of patients coping with chronic illness or disease states (cancer, psoriasis, rheumatoid arthritis, multiple sclerosis) is Leventhal's self-regulatory model (SRM; 1984, 1997). Leventhal and colleagues proposed that patients' illness representations (illness cognitions), in order to make sense of illness experience and health threats, are based around distinct components, which in turn, determine coping and impact on experiences of psychological distress and disability

(Leventhal et al., 1984; Leventhal & Diefenbach, 1991). Illness representation has also been shown to predict decisions to engage in screening behaviours and seek health care (Grunfeld et al., 2003) and to help with coping successfully with chronic illness (Hampson et al., 1990; Schiaffino, et al., 1998).

Illness representations are derived from a number of sources, i.e., personal experiences, past experience with illness, and information obtained from health and social environments. A meta-analysis of empirical studies (n=45) using the model of illness representations found perceptions that the illness is curable/controllable was significantly and positively related to the adaptive outcomes of psychological well-being, social functioning and vitality and negatively related to psychological distress and disease state (Hagger & Orbell, 2003). Specific to breast cancer, Buick (1997) found that illness perceptions were important predictors of psychosocial response to breast cancer treatment (radiotherapy & chemotherapy), independent of objective illness severity. Negative associations between beliefs over control of breast cancer and distress have also been shown in breast cancer patients (Taylor et al., 1984; Buick, 1997).

The self-regulation model has recently been utilised as a framework to understand individual variation in the psychological response to genetic risk of breast cancer (Rees et al., 2004), which provided tentative evidence that both illness perceptions and risk perception contribute independently to different aspects of psychological well-being in individuals at risk of disease. It would appear sensible to use this model to examine individual variations of psychological response in patients completing tamoxifen as patients are likely to have cognitions and expectations of favourable outcomes, i.e., less side effects, non-favourable outcomes, i.e., recurrence of cancer, or both coming to the end of treatment.

Treatment Representations

Another factor that may contribute to distress in patients about to complete tamoxifen therapy is beliefs held about their medicine, i.e., their treatment representations. Researchers examining patient beliefs about illness recently recommended the separation of illness representations from treatment representations to an extended self-regulatory model to better understand patient adherence to medicines (Horne & Weinman, 2002; Hirani & Newman, 2005). This extended model has been successful in predicting medication adherence in other chronic illness populations such as coronary heart disease (Byrne et al., 2005), rheumatoid arthritis (Neame & Hammond, 2005), and asthma (Horne & Weinman, 2002). Horne & Weinman (1999a; 1999b) have shown that beliefs patients hold regarding the necessity of their medication and concerns of adverse effects of medications are weighed as perceived risks and benefits of treatment which is directly related to their level of medication adherence.

Drawing on literature that has examined factors contributing to treatment adherence it may be appropriate to hypothesise that patients who have adhered to tamoxifen for over 4.5 years may be more likely to hold beliefs that the necessity of their medication outweighs their concerns for medication (i.e., adverse side effects), due to recurrence risk reduction. It could also be hypothesised that women with higher concerns of tamoxifen therapy will be less distressed coming to the end of treatment and women with lower concerns of tamoxifen may experience higher levels of distress when treatment ends.

Fear of Recurrence

Reported earlier, one factor that has been found to contribute to distress in patients is fear of recurrence. Percentages of women with breast cancer reporting fears that their disease will recur

range from 60-99% (Curran et al., 1998; Noguchi., et al 1993; Pistrang & Barker, 1992; Polinsky, 1994; Sneeuw et al., 1992). Approximately 70% of survivors still fear the possibility that the disease might recur 5 years after diagnosis (Wong & Bramwell, 1992) and one author has suggested that fear of recurrence is universally present at some level in all patients (O'Neill, 1975). Evidence suggests that fears about recurrence are associated with emotional distress among cancer patients (Sneeuw et al., 1992; Mast, 1998, Moyer & Salvoy, 1998; Walker, 1997) and has been found to be mediated by age and number of significant others in the patient's life (Mast, 1998; Northouse, 1981).

Easterling & Leventhal (1989) suggest that two classes of stimuli may increase the worry about cancer; cues related to the events that have been interpreted as threatening or cues that emphasise the person's mortality (i.e., end of tamoxifen therapy). A number of studies examining the variation of distress in women at increased risk of breast cancer have focused on the accuracy of risk perception and associations between risk perception and the psychological response to risk. These studies have suggested that risk perception is positively associated with cancer specific distress (Lerman et al., 1994; Lloyd et al., 1996; Hopwood et al., 2001; Cull et al., 1999; Watson et al., 1999).

A cognitive model using Leventhal's SRM of illness was proposed to understand patient reactions to the possibility of recurrence (Lee-Jones et al., 1997) that suggests a patients fear of recurrence will vary depending on their illness representation. It is therefore hypothesised that patients with high fears for recurrence will experience higher levels of distress compared to those with lower fears when approaching the end of tamoxifen therapy, given the reduction of recurrence risk when taking tamoxifen.

Personality

Individual differences, other than representations of illness, treatment, fear of recurrence, and adjustment style, such as an underlying personality style, in particular neuroticism, has been postulated to be a contributing factor to health related outcomes as a result of a patients ability to cope with chronic illness (Eysenck & Eysenck, 1985). A review by Williams et al (1997) concluded that neuroticism is a vulnerability factor for psychological morbidity and correlates with measures of anxiety (Jerram & Coleman, 1999). Research has shown neuroticism to be a significant predictor of intrusive anxiety (Tjemsland et al., 1998), psychiatric morbidity (Farragher, 1998), poor outcome (Farragher, 1998), and distress (Millar et al., 2005), in breast cancer patients following diagnosis till two years post-mastectomy. It would seem reasonable to hypothesise that patients approaching the withdrawal of tamoxifen who are already neurotic or anxious, as part of their underlying personality, would be more likely to experience psychological distress due to the reduction of recurrence risk when prescribed tamoxifen, if fearful of recurrence.

Summary of Background

It is evident that factors other than clinical diagnosis and treatment choice contribute to individual variations of distress found in breast cancer patients. Factors demonstrated by researchers contributing to individual variations in adjustment and distress during various stages of breast cancer, have been an individuals adjustment or coping style to their illness, representations of breast cancer illness and treatment, personality characteristics, and fear of cancer recurrence. The degree or incidence of distress found in patients completing tamoxifen therapy, a significant marker in her recovery, is not yet known. In addition, it is not clear whether factors known to contribute to distress at earlier stages of breast cancer diagnosis and intervention are relevant during this period and what weighting they may have on variations of distress.

AIMS & HYPOTHESES

(i) Aims

The current study aims to quantify individual variations of distress in a cohort of women about to complete their 5-year prescription period of tamoxifen adjunctive therapy. It is also the aim of this study to explore relationships between illness representations, treatment representations, adjustment style to cancer, fear of recurrence, and personality, to the level of distress found in women about to end their tamoxifen therapy.

(ii) Hypotheses

1. High levels of distress would be predicted by the nature of treatment representations (lower concerns for effects of tamoxifen).
2. Levels of distress would be predicted by the nature of illness representations (control/cure & timeline acute/chronic).
3. Levels of distress will be mediated by adjustment to cancer coping style.
4. High scores on neuroticism would be associated with high fears of recurrence thus associated with higher distress.
5. Fear of recurrence will be predicted by nature of treatment representations & illness representations.

PLAN OF INVESTIGATION

(i) Participants

Patients who attend the breast cancer clinic that have adhered to tamoxifen therapy and are due to complete their therapy in 1-6 months time will be invited to take part in the study. Participants will have undergone a lumpectomy or mastectomy, chemotherapy or radiotherapy prior to

commencement of tamoxifen therapy. Patients will have been disease-free since commencement on tamoxifen and will be excluded if they are currently undergoing investigation for cancer, is suffering from any other serious illness, learning disability, severe aphasia or where English is not their first language.

(ii) Recruitment

Patients meeting inclusion criteria will be identified by the breast cancer clinic administrative assistant. Pilot investigations with the clinic indicate that approximately 120 potential participants for the study will attend each week. This number is suitable to sample from over a four-month data collection period (approximately 1,920 potential participants, taking into account refusals to participate, exclusions, & drop-outs).

(iii) Measures

To be completed by Researcher

Demographic & Medical Information

Age, postal code data (to calculate DEPCAT scores for socio-economic status), marital status, pre-cancer diagnosis medical & psychiatric history, breast cancer treatment history, procedures performed, and current medication will be collected from medical notes with patient consent.

To be completed by Participant

Distress

The Brief Symptom Inventory (BSI; Derogatis & Melisaraatos, 1983), is a 53-item measure of psychological distress that contains three global scales and nine subscales. Each item is rated on a 5-point Likert scale from 0 (not at all) to 4 (always). Positive cases can be identified by a Global

Severity Index (GSI) score of ≥63 or any two subscales where the *T*-score is ≥ 63 (Derogatis, 1993). The BSI consistently yields a high sensitivity of 0.87 and specificity of 0.89 (Zabora, 1998) and has been utilised in prevalence studies related to psychological distress in oncology patients and breast cancer populations (Stefanek et al., 1987; Zabora et al., 1990; 2001).

Illness perceptions

The Revised Illness Perception Questionnaire (IPQ-R; Moss-Morris et al., 2002) will be used to assess patients' illness perceptions. It is sensitive to beliefs and cognitions about a wide range of chronic illness with a total of eight subscales addressing the components of Leventhal's self-regulatory model: illness identity; acute/chronic time-line perceptions; beliefs in severity of consequences; perceptions of cure or control of the situation; treatment control; illness coherence; cyclical timeline perceptions; and emotional representation of illness. The IPQ-R subscales show good internal reliability, and acceptable levels of stability have been found over 6 weeks and 3 months (correlations ranging from .46 to .88; Moss-Morris et al., 2002). The IPQ has proved to be a significant predictor of distress in patients recovering from breast cancer prior to its revision (Millar et al., 2005).

Treatment representations

The Beliefs about Medicines Questionnaire (BMQ; Horne & Weinman, 1999b) will be used to assess patients cognitive representations regarding the necessity of their medication and concerns they have taking it. The scale has been validated for use in patients with chronic illnesses such as diabetes, renal failure, rheumatoid arthritis, chronic cardiac disease, and oncology outpatient populations (Horne & Weinman, 1999a; 1999b, 2002; Byrne et al., 2005). The BMQ consists of two five-item scales assessing patients' beliefs about the necessity of prescribed medication for

controlling their disease and their concerns about potential adverse consequences for taking it. The questionnaire is a flexible instrument, which can be adapted by changing the reference statement to the desired medication being asked about. A necessity-concerns differential can be calculated as the difference between the necessity and the concerns scales. The internal reliability of the scale is adequate (Cronbach's alpha = .88; Byrne et al., 2005).

Fear of recurrence

The Fear of Recurrence questionnaire (Northouse, 1981), a 22-item 5-point likert response scale, will be used to assess fears of recurrence, as this is the only measure of fear of recurrence in disease-free survivors that has reliability data. The scale includes items such as 'I think about my health often' and 'I am concerned that the difficulties with my illness may not be over'. The measure has been shown to have adequate internal consistency with a small sample (n=30) and has been used widely by other researchers to measure fears of recurrence (Black & White, 2005; Mast, 1998; Walker, 1997) in disease-free survivors.

Adjustment to Cancer Scale

The Mental Adjustment To Cancer Scale (Watson et al., 1988) will be used to assess coping style. The scale assesses coping style corresponding to 5 subscales with good internal consistency (Cronbach's alpha), 'fighting spirit' and 'helpless/hopeless' are amalgamated as they form a bipolar scale (.82), 'fatalism' (.79), 'anxious preoccupation' (.76), and 'avoidance' (a single-item measure that does not constitute a subscale for scoring purposes).

Personality

The Short Scale Eysenck Personality Questionnaire – Revised (EPQ-R; Eysenck & Eysenck, 1985), a 48-item yes/no response format questionnaire, will be used to measure the factors of Psychoticism (P), Extraversion (E), Neuroticism (N) and Lie (L), which have been found to be valid, reliable and replicable across populations and sexes (McKenzie, 1988). Internal consistency scores range from 0.62 to 0.88 (Caruso et al., 2001).

(iv) Design & Procedures

This is a cross-sectional questionnaire design. Patients that meet inclusion criteria will be identified by breast cancer clinic staff. This is to protect patient data from the researcher prior to consenting to participate, in accordance with data protection laws. Patients suitable to take part in the study will be sent an information sheet with a covering letter of support from their breast cancer surgeon 2-3 weeks prior to the patients clinic follow-up appointment. Patients will be asked by their surgeon when attending the clinic if they wish to participate in the study and will be able to discuss any concerns with the clinic staff prior to meeting with the researcher. Patients that consent will meet with the researcher following their clinic consultation. The study will be discussed in full with the patient allowing further questions to be addressed prior to taking part. Participants will be asked to complete 6 questionnaires taking approximately 20-30 minutes, thanked for their participation, and not contacted again. Women identified as having clinically significant levels of distress or psychological morbidity will be offered referral to appropriate services and their breast cancer surgeon and general practitioner will be informed in writing.

(v) Settings and Equipment

Data collection will be carried out in a quiet private room within the breast cancer clinic, at the Glasgow Western Infirmary, following participants follow-up consultation. All data will be stored in a locked filing cabinet and data stored in a PC database will be protected by password to ensure data are confidential. Participants will be allocated identification numbers in order to keep electronic data anonymous. The study will not require specialised equipment other than the questionnaires stated above, and envelopes.

(vi) Power Calculation

The power calculation for this study was calculated using a two-step formula, proposed by Green (1991). Green's (1991) approach is based on Cohen's (1988) power analytic approach and estimates that for a medium effect size (f^2 = 0.15) with 12 predictor variables (age, socioeconomic status, adjustment to cancer (3 scales), fear of recurrence, neuroticism, treatment representations (2 scales), and illness perceptions (3 scales of IPQ-R; timeline acute/chronic, treatment control, personal control), the required sample size to test the hypothesis that the population multiple correlation equals zero with a power of .80 (Alpha = .05) will be 127[1].

(vii) Data Analysis

Data will be analysed using SPSS version-11.5 for Windows. Data will initially be checked for skewness and kurtosis. Data that are not normally distributed will be transformed appropriately. Sample characteristics will be defined using descriptive statistics. Preliminary correlational analyses will be performed to investigate relationships among fears of recurrence, personality construct, adjustment style to cancer, treatment representations, illness representations, to distress and will

[1] Step 1: L= 6.4 + 1.65*m*- .05m^2 therefore L=6.4 + (1.65 X 12) - .05$(12)^2$ therefore L = 6.4 + 19.8 – 7.2 therefore L = 19

ascertain which independent variables should be retained for inclusion in the multiple regression. Age, social deprivation, neuroticism, fear of recurrence, adjustment style to cancer, beliefs about medication, and illness representations, will be entered as explanatory variables in the separate multiple regression analyses, having distress (BSI) as the dependant variable

PRACTICAL APPLICATIONS

If the study is successful in identifying psychological characteristics predicting vulnerability for psychological distress prior to completing tamoxifen therapy, clinical psychologists can consult and educate clinical staff in the routine assessment and monitoring of patients to identify those at risk of distress. Clinical psychology could therefore promote the psychosocial care of disease-free survivors specifically with regard to distress through consultation and direct intervention, encouraging future early interventions to reduce tamoxifen related distress, before significantly impacting on quality of life.

TIMESCALE

Main Study Collection – December to March 2006

Statistical Analysis – April 2006 to May 2006

Write up – May 2006 to July 2006

ETHICAL APPROVAL

Application for ethical approval will be completed and submitted in November 2005.

Step 2: $N \geq L/f^2$ *therefore* $N \geq 19/.15$ therefore $N \geq 126.6666667$

OTHER POTENTIAL PROBLEMS

Participants may be found to have clinically significant levels of distress during the completion of the Brief Symptom Inventory. If this is found to be the case, participants will be given the option for referral to appropriate services and their general practitioner and breast cancer surgeon will be informed in writing. Reporting beliefs about illness and fears for recurrence may exacerbate levels of anxiety or emotional distress surrounding the discontinuance of tamoxifen. If patients become distressed the researcher is trained to reduce acute psychological distress and will ensure the patient is psychologically well prior to departure and will be offered referral to appropriate services for structured intervention.

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AMENDMENTS TO MAJOR RESEARCH PROPOSAL

Amendments prior to ethical submission

1. Hypotheses stated within the proposal were regarded to be inappropriately directional and specific considering the study was investigating questions not previously examined. In addition, the overall aim of the study was to be exploratory in nature and hypotheses stated in the proposal would thus be restrictive. Therefore the hypotheses were amended to: 1. a proportion of patients attending their routine breast cancer follow-up appointment would show clinically significant levels of distress when approaching the end of tamoxifen treatment, and, 2. levels of distress would be predicted by age, cancer treatment history, self reported history of anxiety or depression, socio-demographic factors, and psychological variables (illness and treatment representations, adjustment style, fears of recurrence, and neuroticism). The power calculation was not modified prior to recruitment as the number of variables correlating with distress was not yet known.
2. A visit to the breast clinic highlighted that it would be difficult to access patient medical files to obtain socio-demographic, cancer treatment history, and medical/psychiatric history, due to time constraints between each patient consultation and administration protocols. Therefore it was considered that patient self-report using a semi-structured questionnaire administered by the researcher would be most suitable method to obtain this information (see Appendix 4.7).
3. It was also considered important for patients to rate how they felt about completing tamoxifen as severity of distress could not be attributed solely to tamoxifen withdrawal. Information was obtained by asking patients to rate how anxious, apprehensive, relieved, or positive they were in relation to completing tamoxifen using a four-point Likert scale (see Appendix 4.7).

Amendments following ethical approval

1. Administrative procedures within the outpatient clinic prevented letters of invitation to be sent to potential participants 2-3 weeks prior to their appointment. Case-notes were only available for review between 5-7 days prior to clinic appointment, therefore invitations could only be sent at this time. An amendment to the original ethics application was proposed and approved (see Appendix 3.2).

2. To reduce participation time the main outcome measure within the proposal to measure severity of distress (i.e., Brief Symptom Inventory) was amended to the Brief Symptom Inventory –18. An amendment to the original ethics application was proposed and approved (see Appendix 3.3).

Chapter 4: Major Research Project

Psychological distress in disease-free breast cancer survivors completing tamoxifen therapy: the contribution of illness and treatment representations to psychological morbidity.

Prepared in accordance with requirements for submission to Psycho-Oncology (see Appendix 4.1 for notes for contributors)

Running head: 'Predictors of distress in breast cancer survivors completing tamoxifen therapy'

Submitted in partial fulfilment of the requirements for the Degree of Doctorate in Clinical Psychology.

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Summary

The current study examined the incidence, and factors contributing to, individual variations of distress in a cohort of disease-free breast cancer survivors about to complete tamoxifen therapy. Seventy-two patients, identified through case note review, consented to participate following their non-eventful routine follow-up clinic appointment. Six standardised questionnaires were completed: the Brief Symptom Inventory-18 (BSI-18), Illness Perceptions Questionnaire- Revised (IPQ-R), Beliefs about Medicines Questionnaire (BMQ), Eysenck Personality Questionnaire – Revised (EPQ-R), Mental Adjustment to Cancer Scale (MAC), and Fears of Recurrence Questionnaire (FOR). Six percent of patients showed clinically significant levels of distress when about to complete five-years of tamoxifen therapy. Data were examined using correlation and multiple regression analyses. Multiple regression predicted fifty-eight percent of the variability in global distress scores after using neurotic personality style, concerns about taking tamoxifen, illness perceptions (stronger beliefs regarding severity of consequences, duration, and emotional representations of breast cancer), fears of recurrence, and history of anxiety and/or depression as independent variables. Logistic regression analysis was carried out to ascertain predictors to reliably distinguish between self-reported anxious and non-anxious patients when about to complete tamoxifen therapy. Our regression model significantly accounted for thirty-nine percent of the variance in feeling anxious or not when about to complete tamoxifen with moderate prediction success (72.4% of the anxious patients and 86% for non-anxious patients, for an overall success rate of 80.6%). Clinical and research implications are discussed in relation to the study findings.

Introduction

Breast cancer is the most common incident cancer among women in Scotland [National Health Service in Scotland, 1998]. Evidently, survival from breast cancer has improved over the last 20 years in Scotland, with 56% five year relative survival having been reported for those diagnosed between 1968 and 1972 [Black et al., 1993], compared to 70% for those diagnosed between 1988 and 1992 [Harris et al., 1998]. All women who have oestrogen or progesterone receptor positive early stage breast cancer are prescribed tamoxifen therapy as it has been found to reduce the risk of breast cancer recurrences by 50%, and breast mortality by 28% [Early Breast Cancer Trialists' Collaborative Group, 1998]. Indeed, breast cancer survivors significantly believe in the role of tamoxifen in recurrence prevention [Stewart et al., 2001]. However due to negative outcomes associated with long-term administration (more than five years), such as increased mortality and incidence of uterine and liver cancers [Fisher et al., 2001; Fugh-Berman & Epstein, 1992], women are advised that tamoxifen will be prescribed for a maximum of five years. When tamoxifen is withdrawn, anecdotal evidence from breast cancer surgeons suggest many patients feel extremely anxious at this time due to fears of recurrence. Given the high number of women prescribed tamoxifen (70% of breast cancer patients) it is important to examine the incidence of psychological distress in this population and examine factors that may contribute to individual variation in distress levels.

Breast cancer related distress

Women vary in their emotional responses to diagnosis of breast cancer. It is acknowledged that pre-existing individual adjustment styles can mediate emotional responses at time of initial diagnosis [NHMRC; National Breast Cancer Centre, 2000]. Poor adjustment at diagnosis can compromise psychological health and result in 'clinical distress', encompassing physical, cognitive, and behavioural symptoms of anxiety and depression. Furthermore, cancer-related distress can have an

adverse effect on the patient's adjustment to future cancer-related events (such as adverse treatment protocols). Collectively, between time of diagnosis and up to four years post-surgery, the breast cancer population has been found to have a higher prevalence of distress (40.9%) compared to other oncology patients, such as ear nose and throat cancer patients (32.5%), and have thus been termed as an 'at risk group' for distress [Herschbach et al., 2004]. This however may reflect previous findings that females routinely report significantly more psychological symptoms and express greater levels of distress associated with emotional conflict than males do [Derogatis, 2001].

Despite increasing numbers of patients surviving breast cancer, research investigating psychological morbidity has typically examined factors impacting on adjustment to the diagnosis or early treatment of breast cancer. For example, moderate to high levels of clinical distress have been evident in the immediate aftermath of diagnosis and treatment [Zabora et al., 2001; Fallowfield et al., 1990; Farragher, 1998; Kissane et al., 1998; Steginga et al., 1998] and found to be associated with different treatment and recovery stages [Helgeson et al., 2004; Heim et al., 1997]. The incidence of clinically significant distress has been reported as 25-32.8% at diagnosis and early treatment stages [Zabora et al., 2001; Glanz et al., 1992] and 16.1% one year following surgery [Millar et al., 2005]. Factors found to predict distress severity in response to diagnosis and early treatment are younger age [Schag et al., 1993; Tjemsland et al., 1996; Vinokur et al., 1990; Ganz et al., 1993; Herschbach et al., 2004], a history of stressful life events [Butler et al., 1999], past psychiatric history [Nosarti et al., 2002; Maunsell et al., 1992], number of children under 21 years of age [Ganz et al., 1993; Schag et al., 1993], marital and living status [Omne-Ponten et al., 1992], neurotic personality [Fallowfield et al., 1990; Millar et al., 2005], fears of recurrence [Mast, 1998; Walker, 1997] and illness perceptions independent of illness severity [Buick, 1997; Taylor et al., 1984; Millar et al., 2005].

Other factors that have been associated with severity of distress or poor adjustment throughout diagnosis, treatment, and recovery of breast cancer are social deprivation [Wright et al., 2005; MacLeod et al., 2003; Pinder et al., 1993], chemotherapy [Schover et al., 1995], and adjustment style [Classen et al., 1996; Cotton et al., 1999; Schnoll et al., 1998; Schover et al., 1995; Grassi et al., 1993].

Literature examining distress in survivors of breast cancer (disease-free for five years) is limited as studies include women in markedly disparate time frames following diagnosis and typically examine 'adjustment' in relation to quality of life outcomes, rather than severity of clinical distress. Only one study has examined clinical distress in disease-free post-mastectomy breast cancer survivors and found that the proportion of high psychological distress at eight years did not significantly differ from women never diagnosed with cancer [Dorval et al., 1998]. Age at diagnosis was the only predictor of severity of distress. Another study reported that approximately 90% of women with breast cancer are psychosocially well-adjusted six years after surgical treatment [Omne-Ponten & Sjoden, 1994]. When examining the impact of cancer treatment history to psychosocial adjustment in survivors one study found no differences between breast conservation and mastectomy treatment groups [Omne-Ponten & Sjoden, 1994]. However in another sample of survivors, those treated with chemotherapy, tamoxifen, or both together, were found to be associated with poorer functioning on several dimensions of quality of life compared to those who did not receive adjunctive therapy [Ganz et al., 2002]. Overall however, in contrast to research examining early outcomes the majority of the survivorship literature concludes that there are no major differences in general quality of life measures (e.g., fatigue, social adjustment, sexual functioning) between cancer survivors and healthy controls [Bower et al., 2000; Dorval et al., 1998; Ganz et al., 1996; Ganz et al., 1998; Ganz et al., 2002; Meyerowitz et al., 1999]. This may be a result of adjustment and distress being examined per

'time' post-diagnosis however rather than at time of clinical events or illness stages as particular illness stages, such as recurrence, have been found to be associated with greater distress rather than time post-treatment [Heim et al., 1997].

Factors contributing to distress when completing tamoxifen

Psychological responses when completing tamoxifen therapy is currently unknown. Indeed with regard to any medication withdrawal, we could only find one study that commented on psychological responses to completing disease-modifying medications, which reported that patients felt increased anxiety at this time however responses were not formally assessed [Goodacre & Goodacre, 2004]. Therefore, in addition to factors predictive of cancer-related distress cited in the literature, psychological models of chronic illness and medication adherence and models relating to individual differences in adjustment style and personality, may further our understanding of distress in women completing tamoxifen. These include illness and treatment representations, fear of recurrence, adjustment style and personality.

Illness and treatment representations

Leventhal's self-regulatory model [SRM; Leventhal et al., 1984; 1997] offers a psychological interpretation to understanding distress in response to chronic disease. It has been successful in predicting distress or morbidity in patients with breast cancer and a variety of other chronic illnesses [Hagger & Orbell, 2003]. Leventhal and colleagues proposed that patients' illness representations, in order to make sense of illness experience and health threats, are based around distinct components. These components are illness identity; acute/chronic time-line perceptions; beliefs in severity of consequences; perceptions of cure or control of the situation; treatment control; illness coherence; cyclical timeline perceptions; and emotional representation of illness. It is these

components that form the patient's illness cognitions (or beliefs) that determine adjustment and experience of psychological distress and disability [Leventhal et al., 1984; Leventhal & Diefenbach, 1991]. Specific to breast cancer, illness representations are known and important predictors of psychosocial response to early treatment whereby negative associations have been found between beliefs of control, perceived duration of illness, and symptom awareness to severity of distress [Taylor et al., 1984; Buick, 1997; Millar et al., 2005]. Subsequently when completing tamoxifen therapy beliefs about breast cancer should be considered in relation to psychological responses, however individual beliefs about the drug itself may also mediate psychosocial responses.

The separation of illness representations from treatment representations has recently been recommended to increase the understanding of patient adherence to medicines [Horne & Weinman, 1999a; Hirani & Newman, 2005], as this has been successful in predicting medication adherence in individuals with various chronic illnesses [Byrne et al., 2005; Neame & Hammond, 2005; Horne & Weinman, 2002]. Beliefs about medicines can encompass those relating to the necessity of the medication for health-related outcomes or concerns regarding the medication (due to side-effects or dependence). Indeed, older women holding neutral or negative beliefs about the value of tamoxifen are more likely to discontinue their prescription within two years [Fink et al., 2004], as are women who experience negative side effects [Demissie et al., 2001]. Evidently, it appears that beliefs about the risks and benefits of medicines can be powerful mediators of adherence and therefore may be factors contributing to psychosocial responses when completing tamoxifen. It would seem appropriate to hypothesise that concerns related to taking tamoxifen and beliefs surrounding its necessity would contribute to, or mediate, an individuals psychological response when completing a five-year prescription. For example, patients who have complied with a five-year prescription

(despite experiencing negative side effects) may hold stronger beliefs regarding its necessity and thus experience higher levels of distress on completion.

Fear of breast cancer recurrence

As reported earlier, research has shown that fears about recurrence are associated with emotional distress among cancer patients [Sneeuw et al., 1992; Mast, 1998, Moyer & Salvoy, 1998; Walker, 1997]. Incidence reports suggest that 60-99% of breast cancer patients fear recurrence of disease [Curran et al., 1998; Noguchi et al., 1993; Pistrang & Barker, 1992; Polinsky, 1994; Sneeuw et al., 1992] and approximately 70% of survivors still fear the possibility that the disease might recur five years after diagnosis [Wong & Bramwell, 1992]. Easterling and Leventhal [1989] suggest that two classes of stimuli may increase the worry about cancer recurrence; cues related to the events that have been interpreted as threatening or cues that emphasise the person's mortality. The completion of tamoxifen and beliefs surrounding its disease-modifying quality may be interpreted as such a cue, thus increasing distress.

Adjustment style

Adjustment to cancer can be defined as an ongoing process where the patient tries to manage emotional distress and gain control over ongoing cancer-related life events. Greer and Watson [1987] have identified five common adjustment styles to the diagnosis and treatment of cancer; fighting spirit, avoidance or denial, fatalism, helplessness and hopelessness, and anxious preoccupation [Moorey & Greer, 2002]. Certain adjustment styles, such as fighting spirit, are associated with lower levels of distress in breast cancer patients [Classen et al., 1996; Cotton et al., 1999; Ferrero et al., 1994; Schnoll et al., 1998] and adjustment styles representative of hopelessness/helplessness, anxious preoccupation, and fatalism are associated with higher levels of

distress [Grassi et al., 1993; Schover et al., 1995]. Therefore it would be reasonable to consider adjustment style as a mediator of distress when completing tamoxifen, a significant cancer-related event.

Personality style

Individual differences, such as an underlying personality style, have also been postulated to be a contributing factor to health related outcomes related to patients' ability to adjust with chronic illness [Eysenck et al., 1985]. A neurotic personality style contrasts traits such as nervousness, moodiness, and sensitivity to negative stimuli with coping ability [Rathus & Nevid, 2005, p.62]. Research has shown neuroticism to be a significant predictor of intrusive anxiety [Tjemsland et al., 1998], psychiatric morbidity [Williams et al., 1997], and poor outcome [Farragher, 1998]. Specific to breast cancer, neuroticism has been found to be a predictor of distress at time of diagnosis and up and two years post-mastectomy [Millar et al., 2005]. Given the evidence to suggest that personality, and in particular neuroticism, can mediate the development of distress it would be important to examine its contribution to severity of distress in patients when approaching completion of tamoxifen.

The current study

The current study aimed to quantify individual variations of distress in a cohort of women about to complete their five-year prescription period of tamoxifen adjunctive therapy when attending their routine six-month breast cancer follow-up appointment. Furthermore, it aimed to determine whether factors previously associated with breast cancer distress, at various stages of illness and recovery, are also significant predictors of distress at this time. In addition, it was also intended to explore the

contribution of treatment representations further (i.e., beliefs regarding tamoxifen), to variations of distress.

Hypotheses

1. A proportion of patients attending their routine breast cancer follow-up appointment would show clinically significant levels of distress when approaching the end of tamoxifen treatment.
2. Levels of distress would be predicted by age, cancer treatment history, self reported history of anxiety or depression, socio-demographic status, and psychological variables (illness and treatment representations, adjustment style, fears of recurrence, and neuroticism).

Method

Participants

A power calculation was used to ascertain the sample size required for multiple regression for twelve predictor variables using a two-step formula proposed by Green [1991]. Green's [1991] approach is based on Cohen's [1988] power analytic approach and estimates that for a medium effect size (f^2 = 0.15) with twelve predictors to test the hypothesis that the population multiple correlation equals zero with a power of .80 (Alpha = .05) would be 127.

Seventy-two patients were recruited by means of continuous sampling from patients who attended a 6 monthly follow-up outpatient clinic at a local breast cancer service, Western Infirmary, Glasgow. Patients were eligible to participate if they were about to complete tamoxifen in one to six months time, were not continuing with further adjuvant hormonal therapy (Letrazole), had been disease-free

since commencement on tamoxifen and were not experiencing any other major psychiatric or neurological disease.

Procedure

The present study gained ethical approval from Greater Glasgow Primary Care NHS Health Board and North Glasgow Hospitals University NHS Trust (see Appendix 4.2). Patients were identified as suitable participants from weekly case note file reviews by a specialist breast care nurse. Prior to attending their appointment suitable participants were sent an introduction letter (see Appendix 4.3) and information sheet (see Appendix 4.4) by their consultant and invited to participate. Following a non-eventful clinic appointment, patients were asked by their attending physician if they had questions regarding the study and wished to participate. On obtaining written consent (see Appendix 4.5) patients were interviewed individually by the lead investigator in a private room in the clinic. Cancer treatment and medical history, psychiatric history, and socio- demographic information were obtained by patient report. Patients were asked to complete six self-report psychometric assessment measures (detailed in the *Materials* section below). All participants completed the questionnaires during their outpatient visit. Patients meeting clinical caseness for distress were offered referral to psychological services and their GP and breast surgeon were notified in writing.

Materials

Distress

The Brief Symptom Inventory – 18 [BSI–18; Derogatis, 2001], an eighteen-item instrument is a highly sensitive and efficient screen for psychiatric disorders and psychological distress in medical and cancer patients [Zabora et al., 1990; Zabora et al., 2001; Carlson & Bultz, 2003]. The instrument yields three subscale scores: Somatisation, Depression and Anxiety, which compile a composite

score indicating severity of distress termed 'Global Severity Index' (GSI). Internal consistencies range from .74 to .89. Extensive normative data for oncology and community populations is available.

Illness representations

The Revised Illness Perception Questionnaire (IPQ-R) [Moss-Morris et al., 2002] is a questionnaire sensitive to beliefs and cognitions addressing the components of Leventhal's self-regulatory model. The IPQ-R subscales show good internal reliability, correlations ranging from .46 to .88 [Moss-Morris et al., 2002].

Treatment representations

The Beliefs about Medicines Questionnaire - Specific (BMQ) [Horne & Weinman, 1999b] is sensitive to beliefs surrounding the necessity of a medicine and concerns when taking it. The questionnaire is a flexible instrument, which can be adapted by changing the reference statement to the desired medication being asked about. Questions include 'without tamoxifen I would be very ill' and 'I worry about becoming dependent on tamoxifen'. Consisting of two five-item Likert scales the internal reliability of the scale is adequate [Cronbach's alpha = .88; Byrne et al., 2005].

Fear of recurrence

The Fear of Recurrence questionnaire [Northouse, 1981] is a twenty-two-item five-point Likert response scale measuring severity of recurrence fear. The measure has been shown to have reliability (Cronbach's alpha coefficient of .92) [Hilton, 1989], content validity [Northouse, 1981], and has been used widely by other researchers to measure fears of recurrence [Black & White, 2005; Mast, 1998; Walker, 1997] (see Appendix 4.6).

Adjustment Style

The Mental Adjustment to Cancer Scale [Watson et al., 1988] is a measure designed to assess an individuals' adjustment style corresponding to Greer and Watson's [1987] framework. Consisting of five subscales; 'fighting spirit' and 'helpless/hopeless' are amalgamated as they form a bipolar scale (Cronbach's alpha .82), 'fatalism' (.79), 'anxious preoccupation' (.76), and 'avoidance' (a single-item measure that does not constitute a subscale for scoring purposes), the scale demonstrates good internal consistency [Watson et al., 1988].

Personality

The Short Scale Eysenck Personality Questionnaire – Revised (EPQ-R) [Eysenck et al., 1985], a forty-eight-item yes/no response format questionnaire, measures the personality style of neuroticism. Internal consistency scores range from .62 to .88 (Caruso et al., 2001).

Socio-demographic and clinical information

Age, postal code (to calculate DEPCAT scores for socio-economic deprivation status), number of dependants, psychiatric history, and breast cancer treatment history, was provided by patient report using a semi-structured questionnaire (see Appendix 4.7). Patients were also asked 'how would you describe how you feel about stopping tamoxifen therapy?' Patients rated four psychological responses on a four-point Likert scale (not at all; a little; some; a lot); for feeling apprehensive, positive, anxious, and relieved.

Statistical Analysis

Prior to analysis, all continuous variables were examined for accuracy of data entry, missing values, and fit between their distributions and the assumptions of multivariate analysis (skewness, kurtosis, and homogeneity of variance). The internal consistency and distributions of scales were checked before performing bivariate analyses. Missing values for MAC subscales were replaced by the mean for all cases as missing cases were less than 5% of total cases and did not differ significantly from the sample on any other variable. Three univariate outliers were identified because of their extremely high scores on the BSI-18 Global Severity Index (GSI). Data for the three cases were compared to the complete data set. Examination of univariate outliers did not highlight unusual characteristics and were considered to be from the intended population. Transformation failed to normalise distribution therefore outlier scores were changed to be one unit above the next highest in the data set accordingly [Tabachnick & Fidell, 2001; Field, 2005] to achieve normal distribution (using Kolmogoroc-Smirnov Z test). No multivariate outliers were identified through Mahalanobis distance. Preliminary correlational analyses were performed to investigate relationships between age, socio-demographic status, psychological variables, and distress using Spearman and Pearson correlation coefficient. Preliminary independent t-tests were performed to investigate differences between those reporting feeling anxious or not when about to complete tamoxifen. Multivariate analyses were employed to examine relationships between independent variables and distress and whether reporting feeling anxious or not at completing tamoxifen.

Results

Data completion

Of 95 patients invited to participate, 13 were not suitable to take part in the study due to: cognitive decline (1); intended for continued adjuvant hormonal therapy (10), or stopped tamoxifen

prematurely (2). Of 82 patients suitable to participate 72 took part as 10 refused (12.2%) due to time constraints when attending the clinic.

Patient Characteristics

The demographic characteristics of the 72 patients are illustrated in Table 1.

[Insert Table 1. here]

Sample characteristics were compared to the Scottish breast cancer population diagnosed in 2001. Mean age at diagnosis (M=58.86 SD= 9.89) was similar to that of the general Scottish breast cancer population (M=63.2, SD=14.4) [Scottish Cancer Registry, 2006]. Two thirds of the sample had DEPCAT scores of 4 to 7, reflecting the prevalence of socio-economic deprivation in the sample, however this is similar to other breast cancer research populations in Glasgow [Millar et al., 2005]. Therefore the sample is considered to be representative of the Scottish breast cancer population.

Assessment of Psychological Distress

Mean score and standard deviation for psychological measures are shown in table 2. The mean T score for the Global Severity Index (GSI) measuring distress (BSI-18) was 44.64 (S.D 10.0). Only four (6%) patients met clinical caseness for psychological distress (T score $\geq$63 on GSI or two subscale T scores $\geq$ 63) above community population norms [Derogatis, 2001].

[Insert Table 2. here]

A number of statistical tests were undertaken to examine potential relationships between the psychological outcome measure (GSI), cancer treatment history, history of self-reported anxiety and/or depression, and socio-demographic status. No significant relationships were found between distress and age (Pearson correlation, two-tailed), number of children under 21 years (Pearson correlation, two-tailed), or social deprivation (DEPCAT; Spearman rank correlation, two-tailed). Mean distress scores did not differ according to living or marital status (independent samples t-test, two-tailed) or cancer treatment history (one-way ANOVA). Mean distress scores significantly differed between those who reported a history of anxiety/depression to those who did not (t= 4.529 df=70, p<.001), with higher distress scores found for those reporting a history of anxiety and/or depression.

Further preliminary correlation analyses were carried out to examine co-linearity among independent psychological variables (illness representations, treatment representations, adjustment style, fear of recurrence, and neuroticism), and to ascertain which variables should be retained for inclusion in the multiple regression analyses. Table 3 summarises significant relationships between psychological variables.

The strength of relationships between independent variables (e.g., illness representations, personality, beliefs about medicines and fear of recurrence) and distress ranged from medium to large. As would be expected a high positive correlation was found between global distress and neuroticism, (r=.596, p<.001). Correlations between the scales on the IPQ-R and distress showed that stronger beliefs that breast cancer would last a long time (timeline acute/chronic), had serious consequences, and strong emotional representations of breast cancer were significantly associated

with higher levels of psychological distress when about to complete tamoxifen (r=.307; p= .008; r=.550, .552; p<.001; respectively).

There were also medium positive correlations between concerns about tamoxifen, fears of recurrence, and distress (r= .423, .473; p<.001, respectively). No significant correlations at the 0.01 level were found between distress and adjustment style (MAC subscales), beliefs regarding medicine necessity, and breast cancer representations of personal control, treatment control, and illness coherence.

[Insert Table 3. here]

No variables were considered for exclusion from the multiple regression analyses as no two independent variables had a bivariate correlation of 0.7 or more as recommended by Tabachnick and Fidell [2001, p.83].

Predicting psychological distress

A standard multiple regression was performed between distress (GSI) as the dependant variable and seven predictor variables: self-reported history of anxiety and/or depression, neuroticism, concerns about taking tamoxifen, fears of recurrence, and illness representations of breast cancer (timeline, consequences, emotional representation). Table 3 displays the correlations between the variables, the unstandardised regression coefficients (B), the standardised regression coefficients (β), the semipartial correlations (sri^2) and R^2, and adjusted R^2. R for regression was significantly different from zero, $F(7, 64) = 12.674$, p<.01. Only three of the independent variables contributed significantly to prediction of global distress; neuroticism score (5%), IPQ-R consequences score

(8%), and self-reported history of anxiety and/or depression (5%). The seven independent variables in combination contributed another 40% in shared variability. Altogether, 58% (54% adjusted) of the variability in global distress scores was predicted by knowing scores on these seven variables.

[Insert Table 3. here]

Anxious vs. Non-anxious self-report when completing tamoxifen

Only four participants met clinical caseness for distress (GSI) when about to complete tamoxifen, however in contrast, twenty-nine participants (40%) rated themselves as feeling anxious to some degree on a four-point Likert scale (scores were recoded into two groups: those who reported feeling a little, some, or a lot of anxiety were classified as feeling 'anxious' and those reporting no anxiety at all classified as 'non-anxious'). Further analyses were therefore considered important to examine potential differences between anxious and non-anxious groups and to ascertain if clinical, socio-demographic, or psychological variables were predictors of group membership. Anxious and non-anxious groups were compared on socio-demographic, self-reported history of anxiety and/or depression, and cancer treatment history using crosstabulation Chi-Square tests. Independent sample t-tests for continuous data were used to examine differences between groups on psychological measures and age.

The anxious group were found to have a higher incidence of self-reported history of anxiety and/or depression (34% vs. 13%; x^2= 5.49, df=1, p=.019) and higher global distress scores (GSI; t= 2.763, df= 70, p=0.007) compared to the non-anxious group. Mean age did not differ between groups. Significant differences between groups on psychological continuous variables are shown in table 4. It is evident that those who reported feeling anxious about completing tamoxifen therapy had

significantly higher neuroticism scores, stronger concerns related to taking tamoxifen, stronger beliefs surrounding the necessity of tamoxifen, greater fears of recurrence, stronger emotional representations of breast cancer, and higher scores of anxious preoccupation adjustment style.

[Insert Table 4. here]

A direct logistic regression analysis was performed with self-reported anxiety about completing tamoxifen as the outcome variable, with one clinical history predictor (self-reported history of anxiety/depression), and seven psychological predictors: distress, neuroticism, fear of recurrence, beliefs about medicines (concerns and necessity), emotional representation of breast cancer, and anxious preoccupation adjustment style. A test of the full model with all eight predictors against a constant-only model was statistically reliable, x^2 (8, n=72) = 38.082 $p<.001$, indicating that the predictors, as a set, reliably distinguished between self-reported anxious and non-anxious patients when about to complete tamoxifen. Calculation of R^2 indicates that the model can account for 39% of the variance in feeling anxious or not when about to complete tamoxifen. Prediction success was moderate with 72.4% of the anxious patients and 86% for non-anxious patients, for an overall success rate of 80.6%. Table 5 shows the beta values and their standard errors, Wald statistics, Exp *B*, and 95% confidence intervals for Exp *B,* for each of the eight predictors. According to Wald criterion however, none of the eight predictors reliably predicted self-reported anxiety. Although not statistically significant at the 0.05 level there was a trend towards beliefs surrounding the necessity of tamoxifen contributing to feeling anxious when about to complete therapy.

[Insert Table 5. here]

Discussion

The primary aim of this study was twofold. Firstly, we sought to identify the prevalence of clinical distress in a sample of disease-free breast cancer survivors about to complete adjunctive tamoxifen therapy. Secondly, we aimed to examine the contribution of individual factors to variations of distress, such as beliefs about tamoxifen and other factors known to be contributors to distress at earlier stages of breast cancer. The current study is the first to report the incidence of clinical distress in disease-free breast cancer survivors at five-years and in those about to complete tamoxifen.

There was support for the first hypothesis as 6% of our sample showed clinically significant levels of distress when about to complete five-years of tamoxifen therapy. The incidence of distress found within this sample is lower than incidences found during early treatment (25 to 32.8%) and one-year post-surgery incidences (16.1%). Due to the heterogeneity of methods measuring clinical distress and the duration of disease-free status we are unable to compare our findings to the only other study examining distress in breast cancer survivors at eight years [Dorval et al., 1998]. Nevertheless, the small incidence of those meeting caseness for distress supports previous research findings that approximately 90% of disease-free survivors are psychosocially well-adjusted after surgical treatment [Omne-Ponten & Sjoden, 1994].

There was partial support for the second hypothesis. When factors associated with severity of distress were entered into multiple regression analyses only illness perceptions (perceived consequences resulting from breast cancer), neuroticism, and self-reported history of anxiety and/or depression, significantly accounted for individual variation of distress (18%) in addition to four other variables (40%; fears of recurrence, concerns about taking tamoxifen, emotional and timeline

representations of breast cancer). There was only partial support as age, socio-demographic status, cancer treatment history, adjustment style, and beliefs surrounding the necessity of tamoxifen were not found to be associated with levels of distress as predicted. Variables such as age and social deprivation were not associated with distress at five years and may be a consequence of the sample being relatively older (as the majority of hormone receptor positive breast cancers occur in post-menopausal women) and having higher levels of social deprivation compared to previous studies that include hormone receptor negative and positive breast cancer patients. The majority of our sample was also married with few children aged less than twenty-one years. The finding that cancer treatment history was not associated with distress supports previous findings in the survivorship literature [Omne-Ponten & Sjoden, 1994]. Reasons for adjustment style not being associated with distress using bivariate correlations may be an indication that the MAC scale was not suitable for our sample, as it encompasses constructs theorised to be adjustment styles to cancer, and survivors may not perceive themselves as having to 'adjust to cancer' due to their disease-free status.

Our finding that beliefs surrounding the severity of consequences from breast cancer predicted severity of distress (e.g., 'breast cancer is a serious illness' and 'breast cancer has major consequences on my life'), may suggest that despite time post-treatment and disease-free status consequential beliefs are artefacts of the collective breast cancer experience throughout diagnosis, treatment, and recovery. This may be attributable to actual negative outcomes following breast cancer related-events e.g., having to take early retirement due to fatigue or significant levels of distress resulting in poor adjustment at earlier stages of diagnosis/treatment. Indeed, illness perception components found to predict distress at earlier stages of breast cancer treatment (such as beliefs of control), but not at five-years, may suggest that beliefs surrounding breast cancer may change over time and that early beliefs may not pertain to disease-free survivors due to perceptions

that breast cancer is not a current illness. Our findings provide additional support to Horne & Weinman's [1999a] premise that the separation of treatment and illness representations is useful, not only when examining adherence to medication, but also when examining psychological responses to completing tamoxifen therapy.

Forty-two percent of the variance in distress was unexplained by our model. One possible reason for this would be that a proportion of distress expressed is pre-existing or related to non-cancer-related events, factors not measured or controlled for in the current study. For example, women were not asked whether they were experiencing any current major life events at time of participation and this may have been a contributing factor as a history of other stressful life events [Maunsell et al., 1992] and current marital/sexual problems [Pistrang & Barker, 1995] have both been shown to be predictive to severity of distress.

Following descriptive examination of the data it was also evident that the prevalence of clinical distress was disproportionate to the number of women who reported feeling anxious at the prospect of completing tamoxifen. It was therefore questioned if distress could be attributed to the event being examined (i.e., psychological response to tamoxifen withdrawal), as cross-sectional designs cannot indicate whether distress was pre-existing, or if it was an indication of individual variation in psychological response severity to the event. We therefore compared women who reported feeling anxious at completing tamoxifen to those who did not and found interesting results. For example, factors that were associated with severity of distress e.g., reported history of anxiety and depression, neuroticism, fears of recurrence, concerns regarding tamoxifen, and emotional representations of breast cancer, were also found to be stronger within women who reported feeling anxious in relation to completing tamoxifen. Contrastingly, factors not associated with distress e.g., beliefs regarding

the necessity of tamoxifen and anxious preoccupation adjustment style, were found to significantly differ between women who reported feeling anxious or not, with the anxious group having higher scores on both variables. This may offer some support to our hypothesis that levels of distress may not be attributable to completing tamoxifen per se and should be examined further using a longitudinal design.

Although no one predictor was identified as statistically contributing to predicting whether a woman was anxious or not at completing tamoxifen there was a trend towards those with stronger beliefs surrounding the necessity of tamoxifen to report feeling anxious or not. Indeed, this would seem reasonable as women who remain disease-free may attribute their health status to tamoxifen as it is a recurrence-reduction medication and they would understandably be anxious at its withdrawal. However a larger sample would be required to examine this hypothesis further.

Methodological Limitations

One of the major limitations of the current study was that the sample size was insufficient to meet initial power calculation requirements for twelve predictor variables. Although only seven variables were entered in to multiple regression analyses the sample size remains underpowered using certain power calculations [Green, 1991]. However other papers state that for seven predictors a sample size of 57 would suffice [Harris, 1975] or at least five participants per predictor would be required [Tabachnick & Fidell, 1989]. Nevertheless it is possible that our results are vulnerable to Type II error, in both regression analyses, and variables not identified as contributors to distress, or feeling anxious when completing tamoxifen, may have been unidentified (adjustment style, beliefs regarding necessity of tamoxifen).

It is acknowledged that the BSI-18 may not be sensitive to cognitive worries in breast cancer survivors as some factors associated with feeling anxious were not associated with levels of distress. However this may also be a reflection of the severity of psychological responses in survivors whereby it may be anxiety provoking to complete tamoxifen but perhaps much less so in comparison to a diagnosis of breast cancer or invasive and traumatic treatment protocols. In addition, the method used to classify whether a woman felt anxious or not at completing tamoxifen in the current study can be viewed as arbitrary. Therefore it could be argued that the study may have benefited from the inclusion of questionnaire specifically measuring degree of worry or anxiety when about to complete tamoxifen. This however would have involved devising such a measure, and ensuring its reliability and validity, which was not possible given the time constraints in conducting the study.

It is also acknowledged that the cross-sectional nature of the study only allows for the analysis between distress and psychological factors at a single point in time, thus necessitating some caution in the interpretation of results and inferences about their direction. Nonetheless, the investigation has important implications for the breast cancer population and provides a scientific framework to explore and discuss the anecdotal experiences of clinicians working in this field. Furthermore given the advances in recurrence reduction therapy such as Letrazole, a new pharmaceutical extending adjuvant medication for three years following tamoxifen withdrawal, it would be important to consider the findings of this study and others that will follow when women approach the end of long term (eight years post diagnosis) pharmaceutical therapy.

Clinical & Research Implications

The current study was undertaken as observations from breast surgeons suggested women felt anxious and experienced high levels of distress when about to complete tamoxifen therapy. We have

confirmed this clinical impression using formal measures of distress and self-report. As this is the first study to examine psychological responses in women about to complete tamoxifen therapy, and indeed withdrawal of any medication, clinical implications are preliminary until our findings can be replicated with a larger sample size thus addressing the aforementioned methodological limitations. If our results are replicated then service provision requirements for the management of distressed or anxious patients at time of competing tamoxifen should be considered locally however it would be beneficial to increase awareness of factors predictive of distress and anxiety to assist in the early identification and management of patients. In the interim we recommend that during routine clinic follow-up appointments, breast surgeons, general practitioners, and breast cancer care sisters, should consider asking patients how they feel about completing their tamoxifen therapy in order to address any concerns or anxieties patients may have at this time. This may be especially important when patients are fearful of recurrence and are unaware that continuance of tamoxifen beyond five years increases mortality and risk for cancer recurrence.

It was disappointing to find that neuroticism, a stable personality characteristic [Eysenck & Eysenck, 1991], and a reported history of anxiety and/or depression predicted distress, as neither factor can be altered by psychological intervention. However, it was encouraging that the largest predictor of distress in the current sample were beliefs regarding severity of consequences of breast cancer as these may be mediated using psychological intervention, thus reducing distress.

In conclusion it would seem that the psychological responses of patients to the withdrawal of medications has been neglected within the clinical and research community with medication adherence taking precedence. It is hoped that the current research will initiate other researchers to examine our findings further in breast cancer survivors and in other populations that are prescribed time-limited medications, such as chronic heart failure or rheumatoid arthritis patients.

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TABLE 1. Demographic characteristics, deprivation category (DEPCAT), and clinical treatment history of study participants (n=72)

Age = 62.86 years (S.D = 9.89); range=43-85

	N	%
Marital Status		
Single	5	(6.9)
Married	51	(70.8)
Divorced	3	(4.2)
Widowed	13	(18.1)
Unknown	0	(0)
Living Status		
With others	58	(80.6)
Alone	14	(19.4)
Dependants aged under 21		
No	62	(86.1)
Yes	10	(13.9)
DEPCAT		
1	6	(8.3)
2	9	(12.5)
3	8	(11.1)
4	17	(23.6)
5	7	(9.7)
6	20	(27.8)
7	5	(7.0)
Clinical Treatment History		
Lumpectomy only	1	(1.4)
Mastectomy only	13	(18.0)
Surgery + Adjuvant (chemotherapy/radiotherapy)	58	(80.6)
Self-reported History of Depression and/or Anxiety		
Yes	15	(20.8)
No	57	(79.2)

TABLE 2. Global Severity Index of Distress in BSI-18; IPQ-R; Beliefs about Medicines Questionnaire; MAC; EPQ-R; and Fears of Recurrence mean scores.

	Mean	SD
BSI-18		
Global Severity Index (GSI) of Distress T score	44.64	10.00
IPQ-R		
Acute/Chronic Timeline	14.67	3.26
Consequences	17.10	4.00
Personal Control	19.22	4.16
Treatment Control	20.78	2.27
Illness Coherence	19.36	3.44
Timeline Cyclical	8.68	2.47
Emotional Representation	15.53	4.39
Beliefs about Medicine		
Necessity	13.80	3.78
Concerns	11.15	2.74
MAC		
Fighting Spirit & Helpless/Hopeless	62.28	5.06
Avoidance	1.96	1.0
Fatalism	17.92	3.43
Anxious	20.74	3.43
EPQ-R		
Extraversion	8.01	3.72
Neuroticism	5.54	3.25
Pychoticism	2.49	1.68
Lie	6.72	3.14
Fear of Recurrence	65.10	14.1

TABLE 3. Standard multiple regression of psychological and clinical history variables to Distress

Variables	Distress (DV)	Neuroticism	BMQ-Concerns	Fear of Recurrence	IPQ-R Timeline	IPQ-R Cons	IPQ-R ER	SRH Anx/Dep	B	β	Sr^2 *(unique)*
Neuroticism	.596**	1.000	.343**	.560**	.198**	.297*	.594**	.359**	.021	.320	.05
BMQ-Concerns	.423**	.343**	1.000	.459**	.362**	.320**	.489**	.273**	.007	.096	
Fear of Recurrence	.473**	.560**	.459**	1.000	.397**	.365**	.545**	.314**	.000	.010	
IPQ-R Timeline	.307**	.198**	.362**	.397**	1.000	.454**	.317**	.169**	.001	.017	
IPQ-R Cons	.550**	.297*	.320**	.365**	.454**	1.000	.462**	.211**	.018	.334	.08
IPQ-R ER	.552**	.594**	.489**	.545**	.317**	.462**	1.000	.267**	.005	.099	
SRH Anx/Dep	.476**	.359**	.273**	.314**	.169**	.211**	.267**	1.000	.124	.239	.05

**p<0.01
[a]Unique variability = .18; shared variability = .40

R^2 =.58[a]
Adjusted R^2 =.54
R =.76**

TABLE 4. Significant differences between 'anxious' and 'non-anxious' groups on psychological variables

	Non-anxious Mean (SD)	Anxious Mean (SD)	*t*	df	*p*
BSI-I8 Distress	41.98 (8.10)	47.90 (10.02)	-2.763	70	.007
Neuroticism	4.33 (3.03)	7.34 (2.70)	-4.328	70	.000
BMQ -Concerns	10.35 (2.55)	12.34 (2.60)	-3.232	70	.002
BMQ -Necessity	12.63 (3.53)	15.52 (3.52)	-3.412	70	.001
Fear of Recurrence	58.77 (12.63)	74.48 (10.59)	-5.518	70	.000
MAC- anxious preoccupation	19.81 (3.40)	22.10 (3.05)	-2.920	70	.005
IPQ-R- emotional representation	13.72 (3.74)	18.21 (3.93)	4.892	70	.000

TABLE 5. Logistic multiple regression of psychological and clinical history variables to feeling anxious or non-anxious when completing tamoxifen.

	B	S.E.	Wald	Sig.	Exp(*B*)	95.0% C.I.for EXP(*B*) Lower	Upper
SRH Anx/Dep	1.105	.912	1.467	.226	3.019	.505	18.040
Neuroticism	.149	.143	1.091	.296	1.161	.877	1.537
Distress (GSI)	-3.356	2.335	2.065	.151	.035	.000	3.392
BMQ – Concerns	.030	.152	.038	.845	1.030	.764	1.388
BMQ –Necessity	.187	.101	3.408	.065	1.205	.989	1.470
Fear of Recurrence	.057	.035	2.640	.104	1.058	.988	1.133
MAC- anxious preoccupation	.095	.112	.721	.396	1.100	.883	1.370
IPQR- emotional representation	.181	.115	2.463	.117	1.198	.956	1.502
Constant	-.503	7.754	.004	.948	.605		

R^2= .39 (Hosmer & Lemeshow), Model X^2 (8) = 38.082 p<.001

Chapter 5: Single Case Research Study Abstract

The contribution of performance anxiety to processing efficiency in a cardiac patient with impaired processing speed

Prepared in accordance with requirements for submission to *Neurocase*

Running head: 'Impact of performance anxiety to processing speed'

Address for Correspondence: Leigh Whitnall-Pate, Section of Psychological Medicine, Division of Community Based Sciences, University of Glasgow Academic Centre, Gartnavel Royal Hospital. 1055 Great Western Road, Glasgow G12 0XH, UK. email: Leigh.Whitnall@nhs.net

Submitted in partial fulfilment of the requirements for the Degree of Doctorate in Clinical Psychology.

Abstract

In this paper we investigate the contribution of performance anxiety to impaired processing efficiency according to Eysenck & Calvo's (1992) model of processing efficiency in a cardiac patient using an experimental design. Objective (mean pulse rate) and subjective measures (cognitive interference and anticipatory anxiety) of performance anxiety indicated lower performance anxiety was associated with greater processing speed. Difficulties with interpreting impaired neuropsychological test scores in performance-anxious individuals are discussed and recommendations are made for future research. Clinical implications regarding the adverse impact of performance anxiety on neuropsychological test performance are also discussed in relation to the current limitations surrounding the interpretation of neuropsychological assessment scores.

Appendix 1.1: Discharge coding sheet

Department of Psychological Services and Research

COMPUTER CODING SHEET

Date Ref Rec ..... (Day, Month, Year) ..... [ ][ ][ ][ ][ ][ ]

D.O.B./CHI No. ..... [/]

Pres. Problem	1	2	3	4	5
Problem No. (see coding sheet)					

Chronicity:

1) Less 6 mnths 2) 6 mnths-1 year 3) 1 year or more 4) Not Rated ..... [ ]

Severity:

1) Mild 2) Moderate 3) Severe 4) Not Rated ..... [ ]

Complexity:

1) Not Complex 2) Low Degree 3) Moderate 4) High Degree 5) Not Rated ..... [ ]

Specialty: 1) Adult Mental Health 2) Elderly 3) Learning Disability 4) Neuro 5) Forensic
6) General Medicine 7) Addiction/Substance Misuse 8) Other ..... [ ]

DISCHARGE SECTION

Outcome ..... 1) Much Imp 2) Mod Imp 3) Sl Imp 4) Unchg 5) Det 6) Much Det
7) DNA 8) Seen1/Assess 9) Never Seen 0) Other..... [ ]

Standard Discharge Reason ... 1) Did not opt in 2) Died 3) Failed to attend 4) Never seen [ ]
5) No further improvement possible 6) Parental/client request 7) Problems resolved
8) Transfer to another clinician 9) Transfer to another area 10) Transfer to another agency 11) Treatment complete 12) Unable to attend 13) Inappropriate referral

Date of Discharge (Day, Month, Year) ..... [ ][ ][ ][ ][ ][ ]

Number of attendances ..... [ ]

Appendix 1.2: Differences between geographical area, referring agents and age.

TABLE 1. Mann Whitney-U Test Results: between geographical areas and age of referral.

AREA COMPARED	Statistical Result
AE vs. NU	U= 132948.500, p=0.430
AE vs. WG	U= 30218.000, p=0.317
AE vs. ST	U=28376.000, p=0.172
NU vs. WG	U= 34933.00, p=0.574
NU vs. ST	U= 30904.00, p=0.056
WG vs. ST	U=7005.000, p=0.057

Significance level used $p<0.00083$, calculated using the bonferroni procedure

TABLE 2. Mann Whitney-U Test Results: between referring agents and age of referral.

REFERRING AGENTS COMPARED	Statistical Result
GP vs. CMHT	U= 58981.000, p=0.840
GP vs. PMP	U= 49432.000, p=0.031
CMHT vs. PMP	U= 6468.500, p=0.146

Significance level used $p<0.017$, calculated using the bonferroni procedure

Appendix 1.3: Differences between geographical area, referring agents, and number of sessions attended.

TABLE 1. Mann Whitney-U Test Results: between geographical area and number of sessions attended.

AREA COMPARED	Statistical Result
AE vs. NU	U= 133240.500, p=0.496
AE vs. WG	U= 31679.500, p=0.868
AE vs. ST	U=25285.000, p=0.003
NU vs. WG	U= 34974.00, p=0.584
NU vs. ST	U= 27605.500, p=0.001
WG vs. ST	U=6720.000, p=0.021

Significance level used $p<0.00083$, calculated using the bonferroni procedure

TABLE 2. Mann Whitney-U Test Results: between referring agents and number of sessions attended.

REFERRING AGENTS COMPARED	Statistical Result
GP vs. CMHT	U= 55101.000, p=0.174
GP vs. PMP	U= 55744.000, p=0.895
CMHT vs. PMP	U= 6619.500, p=0.236

Significance level used $p<0.017$, calculated using the bonferroni procedure

Neuropsychology Review

Editor-in-Chief: R. Lazar
ISSN: 1040-7308 (print version)
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Manuscript Style

In general, the Journal follows the recommendations of the 2001 Publication Manual of the American Psychological Association (Fifth Edition). It is strongly suggested that contributors refer to this publication before submitting articles.

All pages should be typed double spaced and numbered (including pages containing the title, author name and affiliation footnotes, abstract, acknowledgments, references, tables, and figure caption list).

A title page is to be provided and should include the title of the article, the authors name (no degrees), the author's affiliation, and suggested running head. The affiliation should comprise the department and institution, as well as the city and state (or nation), and should be typed as a footnote to the author's name. The suggested running head should be less than 60 characters (including spaces) and should comprise the article title or an abbreviated version.

An abstract is to be provided, no longer than 150 words. A list of 5-6 key words is to be provided directly below the abstract. Key words should express the precise content of the article, as they are used for indexing purposes, both internally and externally.

Illustrations (photographs, drawings, diagrams, and charts) are to be numbered in one

consecutive sequence of Arabic numerals and referred to by number in the text. The captions for illustrations should be typed on a separate sheet and should not repeat information already provided in the text. Photographs and figures should be large glossy prints, showing high contrast. Drawings should be prepared with India ink or with a high quality computer program. If using either Excel or PowerPoint, please ensure that axes and other lines are sufficiently thick to be seen clearly if the figure is reduced in size to accommodate journal formatting. Electronic artwork should be in TIFF or EPS format (1200 dpi for line and 300 dpi for half-tones and gray-scale art). Color art should be in the CYMK color space.

Tables should be numbered in one consecutive sequence of Arabic numerals and referred to by number in the text. Each table should be typed on a separate page.

List references alphabetically at the end of the paper and refer to them in the text by name and year in parentheses. Where there are three or more authors, only the first author's name is given in the text, followed by "et al." References should include titles of papers. References should be formatted according to the recommendations of the 2001 Publication Manual of the American Psychological Association (Fifth Edition).

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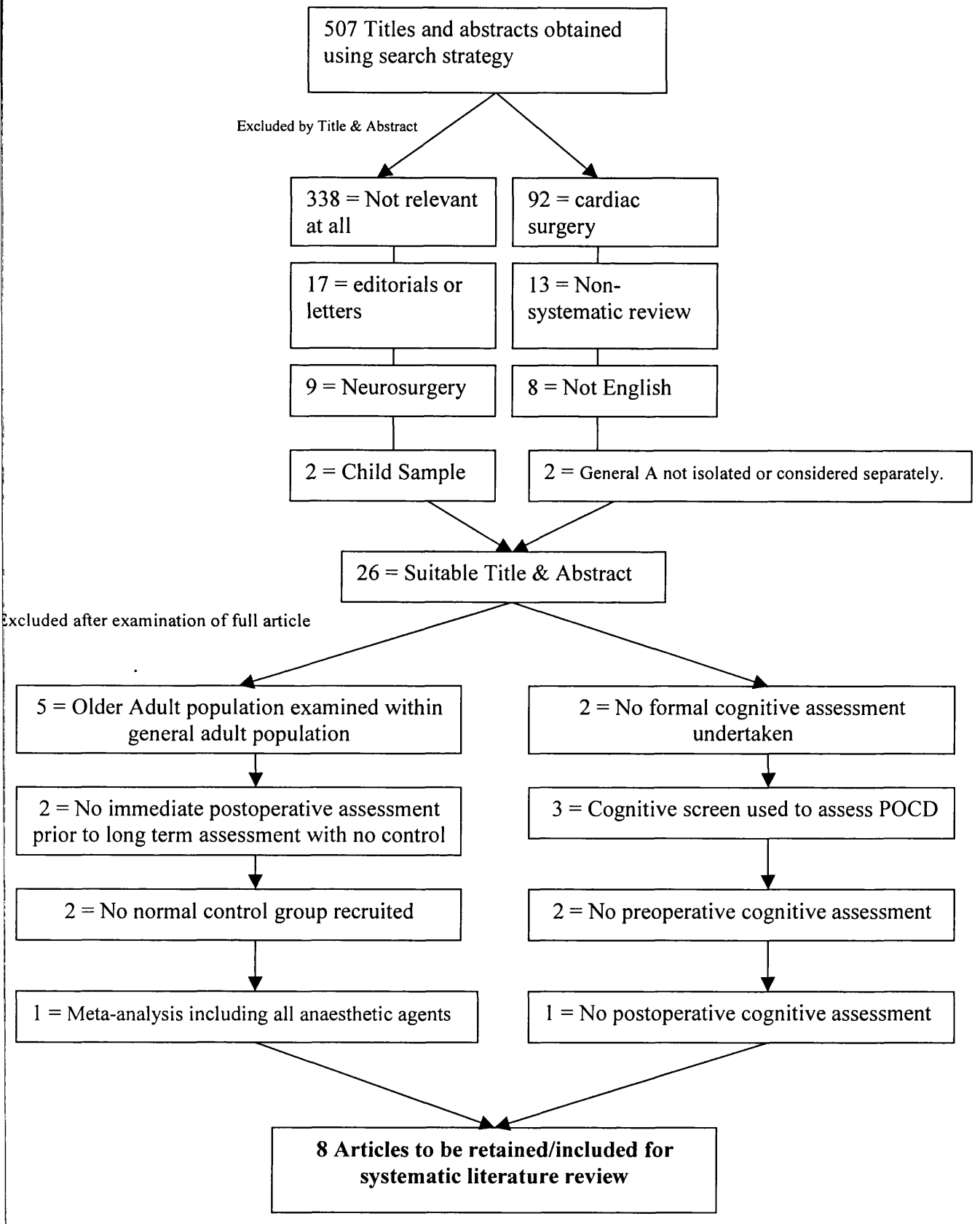
Appendix 2.2: Article selection flowchart



Appendix 2.3: Methodological quality checklist

Study	
Author	
Year	

1. Evaluation Criteria		**Score**
1.1 Does the study have a clearly focused question?		**0 1**
1.2 Does the study have explicit aims?		**0 1**
1.3 Are all the hypotheses stated?		**0 1**
2. Selection of Participants		
2.1 Is the population defined?		**0 1**
2.2 Is the sample size stated?		**0 1**
2.3 Is the sample size justified by a power calculation?		**0 1**
2.4 Are the sample demographics stated?		**0 1**
2.5 Is the sample representative?		**0 1**
2.6 Are all the exclusion criteria **stated?**		**0 1**
2.7 Are all the inclusion criteria **stated?**		**0 1**
2.8 Was a 'normal' non-surgical control group recruited? (to control for a learning effect on test performance)*		**0 2**
2.9 Are cases and controls taken from comparable populations?		**0 1**
2.10 Are the same inclusion/exclusion criteria used for both cases and controls?		**0 1**
3. Procedures		
3.1 Is there adequate randomisation of participants to interventions? 0 = inadequate (use of alternation, case record numbers, birth dates or week days etc) 1 = unclear or not stated 2 = adequate (computer generated random numbers or random number tables)		**0 1 2**

Note criteria followed by a * denotes criteria taken from Statement of Consensus (Murkin et al 1995; 1997).

3.2 Is there adequate blinding? 0 = inadequate (clinician aware of patient allocation) 1 = unclear or not stated 2 = adequate (clinician unaware of patient allocation).		**0 1 2**
3.3 Was the procedure replicable?		**0 1**
4. Assessment		
4.1 Are outcome measures clearly defined?		**0 1**
4.2 Are outcome measures reliable?* 0 = none reliable 1 = some reliable 2 = most/all reliable		**0 1 2**
4.3 Are outcome measures sensitive?* 0 = none sensitive 1 = some sensitive 2 = most/all sensitive		**0 1 2**
4.4 If any assessment/outcome measures are not standardised or are adaptations of standardised assessments, have the reliability and validity statistics been stated? Have adaptations been adequately described? 0 = adaptations not stated or reliability/validity assessed 1 = unclear or not stated 2 = adaptations stated, statistics given, or no adapted assessments used.		**0 1 2**
4.5 Were parallel forms used between re-assessment sessions?* 0 = no 1 = some parallel forms/unclear 2 = all parallel forms		**0 1 2**
4.6 Is the assessment of outcome blind to exposure status?* 0 = inadequate (unblinded) 1 = unclear or not stated 2 = adequate		**0 1 2**
4.7 Is normative data available for appropriate comparisons?		**0 1**
4.8 Was neurologic/neuropsychologic state assessed prior to surgery to obtain an accurate baseline?*		**0 1**
4.9 Were cognitive domains assessed balanced?*		**0 1**
4.10 Are tests free from sex, race, and ethnic bias and structured to avoid floor and ceiling effects?*		**0 1**

Note criteria followed by a * denotes criteria taken from Statement of Consensus (Murkin et al 1995; 1997).

4.11 Were participants assessed by the same qualified and suitable examiner between sessions?*		0 1
4.12 Was care taken to perform at least one assessment when performance is more stable (at least 3 months postoperatively)*		0 1
4.13 Were subjects tested in a quiet, neutral environment to minimise distractions and interruptions?*		0 1
4.14 Were follow-up testing sessions performed in a similar setting and time of day?*		0 1
5. Confounding factors		
5.1 Were most potential confounding demographic factors (e.g., age, sex etc) identified and considered in the design?		0 1
5.2 Was a mood assessment performed concurrently to control for mood influence on test performance?*		0 1
5.3 Were most potential confounding clinical factors (e.g., disease severity, vascular disease, duration of medical illnesses etc) identified and considered in the design?		0 1
5.4 Were most potential confounding demographic factors (e.g., age, sex etc) identified and considered in the analysis?		0 1
5.4 Were most potential confounding clinical factors (e.g., disease severity, vascular disease, duration of medical illnesses etc) identified and considered in the analysis?		0 1
6. Statistical Analysis		
6.1 Do the authors determine whether their groups are comparable and, if necessary, adjust for baseline differences?		0 1
6.2 Are appropriate statistical tests used?		0 1
6.3 Are the results clearly stated?		0 1
6.4 Are confidence intervals provided?		0 1
6.5 Was a learning/practice effect controlled for?		0 1

Note criteria followed by a * denotes criteria taken from Statement of Consensus (Murkin et al 1995; 1997).

6.6 Is there an adequate description of withdrawals? 0 = inadequate or not stated (only numbers, not reasons stated) 1 = partially stated 2 = numbers and reasons provided for each group.		**0 1 2**
6.7 Is POCD identified in individuals using individual change scores rather than group means?*		**0 1**
7. Overall assessment of the study		
7.1 How well was the study done to minimise the risk of bias or confounding, and to establish a causal relationship between exposure and effect? 0 = inadequate 1 = somewhat adequate 2 = adequate		**0 1 2**
7.2 Are the results of the study generalisable?		**0 1**
Total score (maximum = 54)		
Overall %		
Overall Grade		

Note criteria followed by a * denotes criteria taken from Statement of Consensus (Murkin et al 1995; 1997).

Appendix 3.1: Major Research Project Proposal Guidelines

Major Research Proposal

This can be written in the form of an application to a Local Research Ethics Committee and be presented, in full, in the final Research Portfolio. A copy of the letter(s) of ethical approval received from the LREC must also be included in the Research Portfolio. In circumstances where the completed project deviated from the original approved plan, the trainee must insert a clear explanation of these changes. Any further correspondence with the LREC, which relates to such changes must also be appended. The Major Research Project Proposal should include the following headings.

- Full title of project
- Summary of project
- Introduction
- Aims and hypotheses
    - Aims
    - Hypotheses
- Plan of Investigation
    - Participants
    - Participants
    - Recruitment
    - Measures
    - Design and Procedures
    - Settings and Equipment
    - Power Calculation
    - Data Analysis
- Practical Applications
- Timescale
- Ethical Approval
- References

North Glasgow University Hospitals
Division

West Ethics Committee
Western Infirmary
Dumbarton Road
Glasgow G11 6NT

Telephone: 0141 211 6238
Fax: 0141 211 1920

NHS
Greater Glasgow

Date 17th January 2006
Our Ref: AHT/SAJ

Enquiries to Andrea Torrie
Extension As above
Direct Line As above

e-mail address:
Andrea.torrie@northglasgow.scot.nhs.uk

Ms Leigh Witnall-Pate
Section of Psychological Medicine
Gartnavel Royal Hospital
1055 Great Western Road
Glasgow

Dear Ms Whitnall-Pate

Project : 05/S0709/131 Ms L Whitnall-Pate Psychological distress in disease-free breast cancer survivors completing tamoxifen therapy : the contribution of illness and treatment representations of psychological morbidity

The Committee at the meeting on 17th January 2006 noted and approved the content of letter from received 17th December 2005 from you enclosing Notice of Substantial Amendment for the above study

Yours sincerely,

Andrea H Torrie
Manager – West Ethics Committee

POSITIVE ABOUT PEOPLE

01811

Appendix 3.3: Ethical approval letter for substantial amendment 2

North Glasgow University Hospitals
Division

West Ethics Committee
Western Infirmary
Dumbarton Road
Glasgow G11 6NT

Telephone: 0141 211 6238
Fax: 0141 211 1920

NHS
Greater Glasgow

Date 21st February 2006
Our Ref: AHT/SAJ

Enquiries to Andrea Torrie
Extension As above
Direct Line As above

e-mail address:
Andrea.torrie@northglasgow.scot.nhs.uk

Ms Leigh Whitnall-Pate
Section of Psychological Medicine
Gartnavel Royal Hospital
1055 Great Western Road
Glasgow

Dear Ms Whitnall-Pate

Project : 05/S0709/131 Psychological distress in disease-free breast cancer survivors completing tamoxifen therapy : the contribution of illness and treatment representations to psychological morbidity

The Committee noted and approved the content of letter dated 31st January 2006 from you enclosing a Notice of Substantial Amendment to the above study

Yours sincerely,

Andrea H Torrie
Manager – West Ethics Committees

POSITIVE ABOUT DISABLED PEOPLE

01811

Appendix 4.1: Note for contributors to Psych-Oncology

For Authors

Instructions to Authors

Manuscript Submission. *Psycho-Oncology* operates an online submission and peer review system that allows authors to submit articles online and track their progress via a web interface. Please read the remainder of these instructions to authors and then click http://mc.manuscriptcentral.com/pon to navigate to the *Psycho-Oncology* online submission site.

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- The **title page** must list the full title, short title of up to 70 characters and names and affiliations of all authors. Give the full address, including email, telephone and fax, of the author who is to check the proofs.
- Include the name(s) of any **sponsor(s)** of the research contained in the paper, along with **grant number(s)**.
- The current word limit for the journal is, for research articles, **5000** including figures and/or tables but excluding references. For brief reports the limit is **2000** words including no more than two tables or figures and no more than 20 references.

Supply a summary of up to 200 words for all articles [except book reviews]. A summary is a concise summary of the whole paper, not just the conclusions, and is understandable without reference to the rest of the paper. It should contain no citation to other published work.

All abbreviations except for SI symbols should be written in full the first time they appear. Generic or clinical names should be used for all compounds: materials and products should be identified. The species of any animals used should be stated precisely. Sources of unusual materials and chemicals, and the manufacturer and model of equipment should be indicated. Materials and products should be identified in the text by the generic name followed by the trade name in brackets.

Reference Style. References should be quoted in the text as name and year within square brackets and listed at the end of the paper alphabetically. All references must be complete and accurate. Where possible the DOI for the reference should be included at the end of the reference. Online citations should include date of access. Use MedLine abbreviations for journal names. They can be found at: http://www.ncbi.nlm.nih.gov/entrez/jrbrowser.cgi. If necessary, cite unpublished or personal work in the text but do not include it in the reference list. References should be listed in the following style:

Harris CA, Zakowski SG. 2003. Comparisons of Distress in Adolescents of Cancer Patients and Controls. *Pyscho-Oncology* **12:**173-182. DOI:10.1002/pon.631

Cox T, Cox S. 1983. The role of adrenals on the psychophysiology of stress. In *Current Issues in Clinical Psychology,* Karas E. (ed). Plenum Press: London, 3-12.

Lazarus R. 1976. *Patterns of Adjustment.* McGraw-Hill: New York

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- Black and white and colour photos - 300 dpi
- Graphs, drawings, etc - 800 dpi preferred; 600 dpi minimum

- Combinations of photos and drawings (black and white and colour) - 500 dpi

Tables should be part of the main document and should be placed after the references. If the table is created in excel the file should be uploaded separately.

Colour illustrations will not be accepted.

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North Glasgow University Hospitals
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Telephone: 0141 211 6238
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15 November 2005

Ms Leigh Whitnall-Pate
Trainee Clinical Psychologist
Greater Glasgow Primary Care NHS Trust
Section of Psychological Medicine,
1055 Great Western Road
Glasgow G12 0XH

Dear Ms Whitnall-Pate

Full title of study: **Psychological distress in disease-free breast cancer survivors completing tamoxifen therapy: the contribution of illness and treatment representations to psychological morbidity.**
REC reference number: **05/S0709/131**

The Research Ethics Committee reviewed the above application at the meeting held on 15 November 2005. The Committee thanked you for attending the meeting to discuss your study.

The Committee discussed the undernoted with you:

Study design:

a) The Committee wondered if you would be present when the questionnaires are being completed - you replied that this would be the case.
b) The Committee were of the opinion that A10 re null hypotheses had been misunderstood and discussed this with you.
c) The Committee were of the opinion that the questionnaires should be piloted in patients as they thought that these would take "up to an hour" to complete andthat the submission and PIS should be amended appropriately.
d) The Committee thought that you should "pilot" the order of the questionnaires - it may not be appropriate to start with the "anxiety/distress" questionnaire

The Patient Information sheet should be amended as under:

a) GP does not in this instance require to be notified.
b) A further sentence or sentences should be added in respect of "being free not to answer all the questions or all of the questionnaires".
c) A further sentence should be added **in bold** to the effect that "taking part may actually raise some issues which you may previously have not considered".

d) Amend PIS to take into account the revised completion times.

The above minor amendments/clarifications should come back to the Secretary and Chairman for approval.

Ethical opinion

The members of the Committee present gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation.

Ethical review of research sites

The favourable opinion applies to the research sites listed on the attached form.

Conditions of approval

The favourable opinion is given provided that you comply with the conditions set out in the attached document. You are advised to study the conditions carefully.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Application	5.0	31 October 2005
Investigator CV		31 October 2005
Investigator CV Summary (student)		31 October 2005
Protocol	1	31 October 2005
Covering Letter		31 October 2005
Summary/Synopsis		31 October 2005
Peer Review		31 October 2005
Questionnaire		31 October 2005
Letter of invitation to participant		
GP/Consultant Information Sheets	1	31 October 2005
Participant Information Sheet	1	31 October 2005
Participant Consent Form	1	31 October 2005

Research governance approval

The study should not commence at any NHS site until the local Principal Investigator has obtained final research governance approval from the R&D Department for the relevant NHS care organisation.

Membership of the Committee

The members of the Ethics Committee who were present at the meeting are listed on the attached sheet.

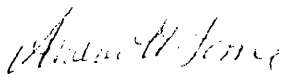
Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

05/S0709/131 **Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project

Yours sincerely



Andrea H Torrie
Ethics Manager – West Ethics Committee

Email: andrea.torrie@northglasgow.scot.nhs.uk

Enclosures: *List of names and professions of members who were present at the meeting and those who submitted written comments*
Standard approval conditions SL-AC2
Site approval form (SF1)

Copy to: R&D Department
Greater Glasgow Primary Care NHS Trust
Research & Development Directorate
Gartnavel Royal Hospital
1055 Great Western Road, Glasgow

North Glasgow University Hospitals
Division

NHS
Greater
Glasgow

West Glasgow Ethics Committee 2
Western Infirmary
Dumbarton Road
Glasgow
G11 6NT

Telephone: 0141 211 6238
Facsimile: 0141 211 1920

13 December 2005

Ms Leigh Whitnall-Pate
Trainee Clinical Psychologist
Greater Glasgow Primary Care NHS Trust
Section of Psychological Medicine, Academic Centre,
1055 Great Western Road
Glasgow G12 0XH

Dear Ms Whitnall-Pate

Full title of study: **Psychological distress in disease-free breast cancer survivors completing tamoxifen therapy: the contribution of illness and treatment representations to psychological morbidity.**
REC reference number: **05/S0709/131**

The REC gave a favourable ethical opinion to this study on 15 November 2005.

Further notification(s) have been received from local site assessor(s) following site-specific assessment. On behalf of the Committee, I am pleased to confirm the extension of the favourable opinion to the new site(s). I attach an updated version of the site approval form, listing all sites with a favourable ethical opinion to conduct the research.

Research governance approval

The Chief Investigator or sponsor should inform the local Principal Investigator at each site of the favourable opinion by sending a copy of this letter and the attached form. The research should not commence at any NHS site until research governance approval from the relevant NHS care organisation has been confirmed.

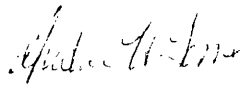
Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating

Procedures for Research Ethics Committees in the UK.

05/S0709/131	**Please quote this number on all correspondence**

Yours sincerely



Mrs Andrea Torrie
Committee Co-ordinator

Email: andrea.torrie@northglasgow.scot.nhs.uk

Enclosure: *Site approval form*

Copy to: Greater Glasgow Primary Care NHS Trust
Research & Development Directorate
Gartnavel Royal Hospital
1055 Great Western Road, Glasgow

West Glasgow Ethics Committee 2

LIST OF SITES WITH A FAVOURABLE ETHICAL OPINION

For all studies requiring site-specific assessment, this form is issued by the main REC to the Chief Investigator and sponsor with the favourable opinion letter and following subsequent notifications from site assessors. For issue 2 onwards, all sites with a favourable opinion are listed, adding the new sites approved.

REC reference number:	05/S0709/131	**Issue number:**	2	**Date of issue:**	13 December 2005
Chief Investigator:	Ms Leigh Whitnall-Pate				
Full title of study:	Psychological distress in disease-free breast cancer survivors completing tamoxifen therapy: the contribution of illness and treatment representations to psychological morbidity.				

This study was given a favourable ethical opinion by West Glasgow Ethics Committee 2 on 15 November 2005. The favourable opinion is extended to each of the sites listed below. The research may commence at each NHS site when management approval from the relevant NHS care organisation has been confirmed.

Principal Investigator	*Post*	*Research site*	*Site assessor*	*Date of favourable opinion for this site*	*Notes* [1]
Ms Leigh Whitnall-Pate	Trainee Clinical Psychologist	Greater Glasgow NHS Health Board	West Glasgow Ethics Committee 2	15/11/2005	
Ms Leigh Whitnall-Pate		Greater Glasgow NHS Health Board	NHS Greater Glasgow Primary Care Division (Community & Mental Health)	13/12/2005	

Approved by the Chair on behalf of the REC:

..... (Signature of ~~Chair~~/Administrator)

(delete as applicable)

..... (Name)

[1] *The notes column may be used by the main REC to record the early closure or withdrawal of a site (where notified by the Chief Investigator or sponsor), the suspension of termination of the favourable opinion for an individual site, or any other relevant development. The date should be recorded.*

North Glasgow University Hospitals
Division

NHS
Greater
Glasgow

<Date>

Dear Madam

'Patient attitudes associated with stopping tamoxifen treatment'

As you have been taking tamoxifen for over 4 ½ years and are about to attend the breast cancer clinic for a follow-up appointment at the Western Infirmary I am writing to ask if you would consider participating in the above research study which is being carried out in the clinic.

I have enclosed an information sheet detailing the background of the study, what would be asked of you if you decide to take part, and other questions you may have about taking part in the study. The research study is being conducted by the Section of Psychological Medicine at the University of Glasgow.

If, after reading the information sheet, you are interested in taking part in the study, and I have discussed your participation with you at your clinic appointment the researcher will meet with you at the clinic after your follow-up consultation. Taking part will involve meeting the researcher for 20-30 minutes after your appointment on one occasion only. You can ask any questions regarding this study by telephoning the researcher Leigh Whitnall on **0779 505 5143** or by meeting her at the clinic before taking part. Meeting or speaking with the researcher will NOT commit you to taking part in the study.

I would like to take this opportunity to thank you for taking the time to read this letter.

Yours sincerely

Professor W D George
Consultant Breast Surgeon
Return Breast Clinic

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GLASGOW

PATIENT INFORMATION SHEET

Study Title

Patient attitudes associated with stopping tamoxifen treatment.

Introduction

You are being invited to take part in a research study. Before you decide whether you want to take part it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information and discuss it with friends or relatives. If you would like more information or there is anything that is not clear please ask us. Take time to decide whether or not you wish to take part.

Thank you for reading this information sheet.

What is the purpose of the study?

A large number of women diagnosed with breast cancer have been prescribed tamoxifen for a period of 5 years. It has been observed in some clinics that women vary in their attitudes to stopping tamoxifen treatment. The intention of our research is to examine various psychological factors to see if they explain variation in women's attitudes.

Why have I been chosen?

This study is specifically looking at women that are about to stop taking tamoxifen, after taking it for nearly five years. As you are due to attend the breast cancer clinic for your follow-up appointment and have been taking tamoxifen for 4 ½ years or more, you have been chosen to be invited to take part.

Do I have to take part?

No. It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will **not** affect the standard of care you receive.

What will happen to me if I take part?

During your clinic appointment the breast cancer surgeon will ask if you would like to take part in the study and if you have any questions about the study. If you are willing to take part you will meet with the researcher, Leigh Whitnall, after your clinic appointment in the next room. If you consent to taking part in the study you will be asked to fill in some questionnaires about your mood, personality, coping style, and beliefs about cancer and tamoxifen therapy. You will also be asked some questions about yourself and how you are, being free not to answer all the questions or all of the questionnaires. This should take approximately 20-30 minutes. Taking part may raise some issues, which you may previously not have considered.

PSYCHOLOGICAL MEDICINE
Division of Community Based Sciences
Academic Centre, Gartnavel Royal Hospital, 1055 Great Western Road, Glasgow G12 0XH

Head of Section of Psychological Medicine: Dr Elizabeth A Campbell

What are the possible benefits of taking part?

There are no direct benefits for you by taking part in this study. However, the information we get from this study may help us to understand better women's varying attitudes to stopping tamoxifen.

Will my taking part in this study be kept confidential?

All information received will be completely confidential and known only to the research workers and names of patients will not be divulged to any other person without further consent. Your GP and breast cancer team will be notified of your participation, with your consent, in writing by the researcher. Any information about you that leaves the hospital will have your name and address removed so that you cannot be recognised from it and will be stored in locked filing cabinets.

What will happen to the results of the research study?

The researcher will write up the results of the research study. A summary of results can be provided to you if requested. You will not be identified in any reports or publications.

Who is organising and funding the research?

Leigh Whitnall, Trainee Clinical Psychologist and Professor Keith Millar from the Section of Psychological Medicine at Glasgow University together with Dr Sharon Mulhern, Clinical Psychologist, and Professor Craig White, Consultant Clinical Psychologist from the Cancer Distress Management Project in Ayrshire, are the organisers of the research. The study is funded by the Section of Psychological Medicine as part of the training requirements of Leigh Whitnall's Doctorate in Clinical Psychology. If you agree to take part you will not incur any expense.

Contact for further information

If you have any questions about the study please contact Leigh Whitnall, Trainee Clinical Psychologist on 07795055142 or email lw57j@clinmed.gla.ac.uk

Thank you for considering this invitation to participate in the research study.

Complaints

If you want to make a complaint regarding the receipt of this information, or its contents, you can telephone the Western Infirmary Complaints Officer on 0141 211 2257 or 0141 211 2926.

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Patient Identification Number for this Study:

CONSENT FORM

Title of Project: **Patient Attitudes associated with stopping Tamoxifen Treatment**

Name of Researcher: **Leigh Whitnall**

Please Initial Box

1. I confirm that I have read and understood the information sheet dated..... (version.....) for the above study and have had the opportunity to ask questions. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving reason, without my medical care or legal rights being affected. ☐

3. I give permission for the researcher to notify my General Practitioner and Breast Cancer Clinic team members that I am participating in this research. ☐

4. I agree to take part in the above study. ☐

Name of Patient	Date	Signature
Name of Person taking consent (if different from researcher)	Date	Signature
Researcher	Date	Signature

PSYCHOLOGICAL MEDICINE
Division of Community Based Sciences
Academic Centre, Gartnavel Royal Hospital, 1055 Great Western Road, Glasgow G12 0XH
Head of Section of Psychological Medicine: Dr Elizabeth A Campbell

Fear of Recurrence Questionnaire.

Check the answer which best typifies your response to the statement.

	Strongly agree	Agree	Neutral	Disagree	Strongly Disagree
1. I think about my health often.					
2. I am bothered by the uncertainty of my health status.					
3. I think more about my health now than before my cancer was diagnosed.					
4. I have no physical concerns at this time.					
5. I worry more about my health than other people worry about their health.					
6. I feel that there is little need to worry about my future health status.					
7. I always take my health into consideration when making future plans.					
8. Compared to other persons who have cancer, I feel that I worry less than they do about health concerns.					
9. My future health status is not a major concern of mine.					
10. I sometimes find myself preoccupied with my physical condition.					
11. Just prior to regularly scheduled exams, my uneasiness about my health increases.					
12. I think no more about my health presently than I did before my cancer was diagnosed.					
13. I am not bothered by uncertainty regarding my health status.					
14. I would like to feel more certain about my health.					
15. I seldom think about my health.					
16. Because of my physical health, my future is of concern to me.					
17. I do not worry about my cancer returning.					
18. When I think about my future health status, I feel some uneasiness.					
19. Minor aches and pains remind me of my cancer.					
20. I feel optimistic as I focus on my future.					
21. I am concerned that the difficulties with my cancer may not be over.					
22. I do not feel anxious about my future when I read articles about my cancer.					

Appendix 4.7: Semi-structured questionnaire

Semi-structured interview to be carried out by chief investigator prior to completion of questionnaires.

Socio-Demographic Information

Participant ID		Postal Code	

DOB		Age	

Marital Status (circle)	Single Separated Divorced Widowed Married Other	No of children <21 yrs Live Alone?	 **Yes / No**

Treatment History

Treatment	Received as part of treatment	Date of procedure/ treatment completed
Lumpectomy	**Yes / No**	
Mastectomy	**Yes / No**	
Chemotherapy	**Yes / No**	
Radiotherapy	**Yes / No**	
Neoadjuvant/Endocrine	**Yes / No**	
Other	**Yes / No**	

Medical History

Significant medical history (e.g., other advanced disease, chronic illness, hospitalisations)	Yes / No If yes, please state more detail.
Significant psychiatric history (e.g., history of anxiety, depression, Bipolar disorder, or psychosis that was treated by medication or talking therapy.	Yes / No If yes, please state more detail.
History of alcohol/substance abuse	Yes / No
Current alcohol/substance abuse	Yes / No

Response to Completing Tamoxifen

How would you describe how you feel about coming off Tamoxifen in the next 6 months?

Apprehensive	Not at all	A Little	Some	A lot
Relief	Not at all	A Little	Some	A lot
Anxious	Not at all	A Little	Some	A lot
Positive	Not at all	A Little	Some	A lot

Have you taken tamoxifen as prescribed by your surgeon i.e., have you taken it as per their advice during the last 4.5 years? **Yes / No**
If no, please state why:

_____
_____
_____

Have there been times where you did not take tamoxifen? **Yes / No**
If yes, please state why-

_____
_____