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**Emotional sequelae during and following hospital admission for
diabetic ketoacidosis**

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in Partial Fulfilment of the Requirements for the Degree of
Doctorate in Clinical Psychology
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D. Clin. Psychol. Declaration of own work

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1. THESIS ABSTRACT

Increasingly patients are surviving admission to intensive care units (ICUs) with life-threatening, critical illness. This has led to a growing interest in longer-term patient outcomes, including their psychological health.

This thesis consists of two discrete sections: 1) a systematic review of research that evaluated emotional outcomes between 3 and 12 months post-ICU discharge, and 2) a longitudinal cohort study of emotional sequelae among adults with Type 1 diabetes during and following admission for diabetic ketoacidosis (DKA).

The systematic review identified seven studies that met inclusion criteria, and highlighted weaknesses in the existing literature. From the available evidence there appears to be elevated rates of clinically significant depression (11%), anxiety (15%) and post-traumatic stress disorder (PTSD) symptoms (23%) 3 months after discharge, and these remain high 9 months later (12%; 18%, and 27%, respectively).

The prospective study of DKA admissions indicated substantial rates of clinically relevant depression (25%); anxiety (37.5%), and PTSD symptoms (37.5%) prior to discharge. However, 3 months later the rates of depression and PTSD had substantially attenuated (both 8.3%) although rates of anxiety (37.5%) remained higher than that found in the general population (7%) and the local Type 1 diabetes clinical community (11.9%). Those admitted with DKA had significantly poorer HbA_{1c} compared to the overall Type 1 clinic population (10.9% vs. 8.9%; $p < 0.0001$), which indicates substantial difficulties in self managing their condition.

It appears that psychological problems are elevated over time following ICU discharge. PTSD is notably high and enduring in general ICU survivors, whereas was observed to fall away in the DKA sample. Anxiety seems to be elevated and this persists over time following DKA; this is pertinent given the dearth of research on the role of anxiety in the efforts of people with type 1 diabetes to manage their condition. As far as the authors' are aware, this is the first study tracking emotional

outcomes post DKA discharge. There are clearly significant psychological issues that will likely impact on staff efforts to provide ward-based care aimed at improving post-discharge diabetes control, and on the future efforts of those admitted for DKA to self-manage a complex condition. A greater awareness of the psychological issues affecting people with type 1 diabetes who experience DKA is an important first step. More specifically, a better understanding among health professionals about the ways emotional distress can impact on self-management is needed, as well as a greater understanding of how best to communicate information and educational material in light of possible information processing deficits (which may be a result of emotional distress). Larger, multi-centre, higher quality studies are required in both general ICU settings and looking at specific disease complications (such as DKA). Psychological screening for ICU survivors and implementation of a care pathway to allow access to services post-ICU may be a useful development.

2. THESIS OVERVIEW

This thesis consists of a systematic review of research that evaluated psychological outcomes between 3 and 12 months post-ICU discharge. This review has been presented in the format required by the journal, *Journal of Critical Care*. A bridging chapter then introduces the quantitative research project. The methods of this research project are described in detail. This is a prospective longitudinal cohort study of emotional sequelae among adults with Type 1 diabetes during and following admission for DKA. It is provided as a journal article, in the format required by *Diabetes Care*. The guidelines for submissions to both journals are included in Appendix 1 and 2 respectively.

3. SYSTEMATIC REVIEW

Emotional outcomes following discharge from intensive care:

A systematic review ✧, ✧ ✧

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ABSTRACT

Purpose

To systematically review studies evaluating the emotional outcome of Intensive Care Unit (ICU) survivors between 3 and 12 months post-discharge.

Methods

A systematic review was performed using Medline, EMBASE, CINAHL and PsycINFO. Reference lists from all included studies were also screened.

Results

Seven articles met eligibility criteria. The mean scores at baseline were below case levels for anxiety and depression (7.23 and 6.30 in the Hospital Anxiety and Depression Scale, respectively) and at 6 months were again non-case levels for anxiety, depression and post-traumatic stress disorder (PTSD) respectively. The mean clinical caseness for anxiety, depression and PTSD symptoms were 15%, 11% and 23% at 3 months and 18%, 12% and 27% at 12 months respectively. No significant change over time was observed for levels of emotional distress in the majority of studies.

Conclusions

The acute stress reaction typically reported following non-ICU traumatic events up to 3 months was not observed, however emotional distress does not appear to attenuate from 1 to 12 month follow-up and the reasons for this are unclear. Although larger, multi-centre, higher quality studies are needed, as well as a widely-accepted methodological quality criterion, it is apparent that ICU survivors require both psychological and physical care.

Keywords

Critical care; anxiety; depression; posttraumatic stress disorder-related symptoms; stress

3.1 Introduction

Many adults are admitted to intensive care units (ICUs) throughout the UK every year. For example, there have been about 35,000 admissions per year to ICUs in Scotland over the past decade or so [1]. The presenting nature of critical illness to ICU is heterogeneous, however, always life-threatening [2]. Abnormalities in respiratory rate and suctioning pain are commonplace, as well as hypothalamic-pituitary-adrenal strain and circadian rhythm sleep disorder [2].

Regular physiological observations of patients are required and this can frequently include invasive monitoring of heart rate, oxygen saturation and temperature [2]. Sedation for pain alleviation is routine and various invasive or interventional procedures are carried out while patients are in critical care, including mechanical ventilation and emergency surgical procedures [2]. Patients often have limited ability to communicate; experience loss of control of their bodily functions; suffer periods of impaired cognition (including confusion and delirium), and reduced autonomy during and after administration of these treatments [2]. Moreover, a patient experiencing some or all of these symptoms may likely have difficulties interacting with staff and visitors, which has been demonstrated to increase frustration and perceived isolation [3].

The numbers of people surviving admission to ICUs continues to improve. In the last decade, the inpatient mortality rate has decreased from about 33% to 25% [1]. For many patients recuperation is relatively uncomplicated but for others, discharge from ICU is the start of an uncertain journey towards recovery. Recovery from illness is highly individual, and few studies have been able to demonstrate a close relationship between specific features of an acute illness and its longer-term impact [4]. As one may expect, patients who have had more prolonged episodes of critical illness are likely to have greater long-term difficulties [4], however, patients with even relatively short ICU stays may also need substantial help. Whilst many patients recover to previous levels of functioning [5], some patients experience persistent problems or develop new difficulties after their ICU stay, which can impact on many aspects of their life. In short, life may change in profound ways for ICU survivors.

For example, often survivors have to reduce their hours of employment or give up their jobs due to physical limitations and this will impact on their economic situation [5]. Moreover, some may become dependent on others to carry out activities of daily living which may fundamentally alter their relationships with family and friends [5, 6].

Traditionally, rehabilitation after ICU focussed on physical functioning [4] because physical weakness and reduced mobility are commonplace after prolonged intensive care [2]. However, over recent times there has been an increasing focus on psychological outcomes, which in part reflects a greater emphasis within healthcare of holistic, person-centred care. Emerging research suggests that the ICU experience itself and the combined post-discharge effects of critical illness can have a negative impact on emotional wellbeing, quality of life and neuropsychological outcomes [7,8] . Previous systematic reviews cite median point prevalence rates of 28% (range 8 to 57%) for depression (1 to 21 months post discharge) [9], and 22% (range 0 to 62%) for post traumatic stress disorder (PTSD; 2-120 months post discharge) [10], experienced by patients following ICU admission.

Recently, researchers have become increasingly interested in PTSD and PTSD symptoms post-ICU discharge [10]. PTSD is characterised by a triad of symptoms (internally re-experiencing the traumatic event; avoidance of situations that are associated with the traumatic event, and hyper-arousal of the autonomic nervous system) causing significant distress and impairment in day-to-day functioning. Although the potential for a post-traumatic psychological reaction following critical illness is not in doubt, it is important that rather than focusing on a single mental health condition, researchers and clinicians are mindful of emotional distress in a broader sense [11]. This is partly because it is widely known that approximately 80% of PTSD cases arise in the context of clinically significant co-morbid psychological problems [12]. Most commonly, anxiety disorders and depression co-occur with PTSD (in about 55% and 50% of cases, respectively [12]). There is also debate about the validity of differentiating among these clinical diagnoses due to significant symptom overlap. For example, diminished interest in previously enjoyable activities

and sleep difficulties are symptoms of both PTSD and depression; whereas irritability and hyper-vigilance are indicators of PTSD and other anxiety disorders [12,13,14]. It is also important to note that both anxiety and depression can commonly occur after trauma without PTSD or with sub-clinical levels of PTSD symptoms [12]. Although there have been systematic reviews of depression and of PTSD symptoms in patients following ICU discharge, there are many limitations to this research. Importantly, the vast heterogeneity of populations studied means it is very difficult for the reader to make valid or reliable conclusions. For example, one review [10] compares a general ICU in Turkey two months post discharge with a sample in Sweden of medical trauma admissions 118 months post discharge. In this systematic review the authors' wanted to look at the same samples admitted to general ICU across time so they acted as their own controls and to enable the course of clinical caseness to be clearer. Furthermore, a minimum of three months follow-up was imposed in order to reduce the likelihood of any acute reaction skewing the results (which is typically seen in general trauma literature [14]). Studies which reported PTSD and anxiety and depression were reviewed over time in order to see if there is a possibility of symptom overlap. As far as the authors' are aware there has been no systematic review exploring more generally the emotional outcomes (defined as PTSD and anxiety and depression herein) of this group. Therefore, the aim of this review is to evaluate systematically the symptoms of PTSD, anxiety, and depression among ICU survivors between 3 and 12 months post-discharge.

3.2 Methods

3.2.1 Search strategy

The main search to identify relevant studies was conducted in July (week 23) of 2012. The Cochrane Library was searched to identify any previous systematic reviews of emotional distress encompassing PTSD symptoms, anxiety and depression measures; none were identified.

The following databases were then searched using EBSCOhost: Medline (2000-week 29 2012); EMBASE (2000- week 29 2012); CINAHL (2000- week 29 2012); and PsycINFO (2000- week 29 2012).

The search strategy included the following terms mapped to the appropriate keywords (“Stress, Disorders Post-Traumatic” OR “anxiety” OR “depression”) AND (“critical care” OR “intensive care units” OR “intensive care”). The search boxes “English language” and “human” were also ticked.

3.2.2 Study selection

Articles were selected for review if they met all of the following criteria:-

- The study population was composed of an adult (≥ 18 years) ICU population.
- PTSD and anxiety and depression assessments were conducted using validated measures at a minimum of 3 months and maximum of 12 month follow-up post ICU discharge.
- The study was published in English.

Unpublished articles were not included. In addition, studies reporting on the following conditions/events were also excluded: transplants, natural disasters, physical trauma populations in isolation (including RTA/ burns), war veterans, chronic pain, Guillain-Barre Syndrome, pregnancy / post-partum, elective surgery, cancers and neurological conditions such as stroke and brain injury.

One rater (KYM), sequentially reviewed citations, abstracts and full-text articles to select eligible studies. Reference lists from all included studies were screened by the reviewer to search for further papers.

3.2.3 Data abstraction

For each eligible study, information was abstracted regarding characteristics of the study cohorts, PTSD, anxiety, and depression measures. Authors of eligible studies were contacted for additional information, when necessary. The mean prevalence rates of clinically significant levels (or caseness) for anxiety; depression and PTSD were calculated and plotted. Hospital Anxiety and Depression Scale (HADS; 15) anxiety or depression scores of 11 or greater were considered as clinical cases. This conservative threshold is a deviation from other authors' recommendations [e.g. 16],

and although it may reduce the sensitivity, it reduced the likelihood of inflated prevalence rates and is in keeping with standard clinical practice. A linear trend line was also plotted to explore levels of clinical caseness post-ICU. One of the main ways PTSD differs from other anxiety disorders is that for most people it is often characterised by a progressive reduction of symptoms over time. One area where there has been significant research and an extreme PTSD course is rape and therefore, for reference, the rate of PTSD symptoms following rape [17] was plotted. Absolute numbers of those meeting clinical levels of PTSD, anxiety and depression were reported. In one article, data was drawn from the control group of randomised controlled trials (RCTs).

3.2.4 Methods of reviewing studies

We have discriminated between reporting and methodological quality as proposed by da Costa [18].

Reporting quality herein is defined as “the completeness with which a study is presented and whether major items for the proper appraisal of internal and external validity of findings are clearly reported” (Williams, 2010). The Strengthening in Reporting of Observational Studies in Epidemiology [STROBE; 19; further detail in Appendix 3] statement is used to assess the reporting quality.

Methodological quality herein refers to the “appropriateness of the methods employed in the design and conduct of epidemiological research, which determines the reliability of findings” [18]. A wide range of methodological quality criteria were considered however many were neither valid nor reliable for observational studies [e.g. 20, 21, 22]. From the literature [e.g. 23, 24], expert opinion (Cochrane Collaboration Bias Group) and personal communication with the authors of previous systematic reviews (personal communications, 18 January 2012) in field there appears to be no consensus or standardised methodological quality criteria of observational studies. Therefore in this study key methodological components impacting the systematic review question are discussed and critically appraised within the results section which is consistent with a recent systematic review of

observational studies stating that studies should be considered based on individual quality components [23] rather than on summary scores which involve inherent weighting of component items which have been deemed both variable and inconsistent [24].

The raters (KYM and AK) calculated inter-observer agreement for data abstraction using intra-rater co-efficient. In addition mean scores of anxiety, depression and post PTSD were collated from the studies or additional information from the authors.

3.3 Results

3.3.1 Search results

Appendix 4 details the search results from each database. As illustrated in Figure 3.1, the full texts of 45 studies were evaluated independently by two raters (the first and second authors). There was 100% inter-rater agreement that eight articles were eligible for data abstraction. One article [25] used a total score for the HADS and the authors did not respond to requests for individual anxiety and depression scale scores, so this article was subsequently excluded.

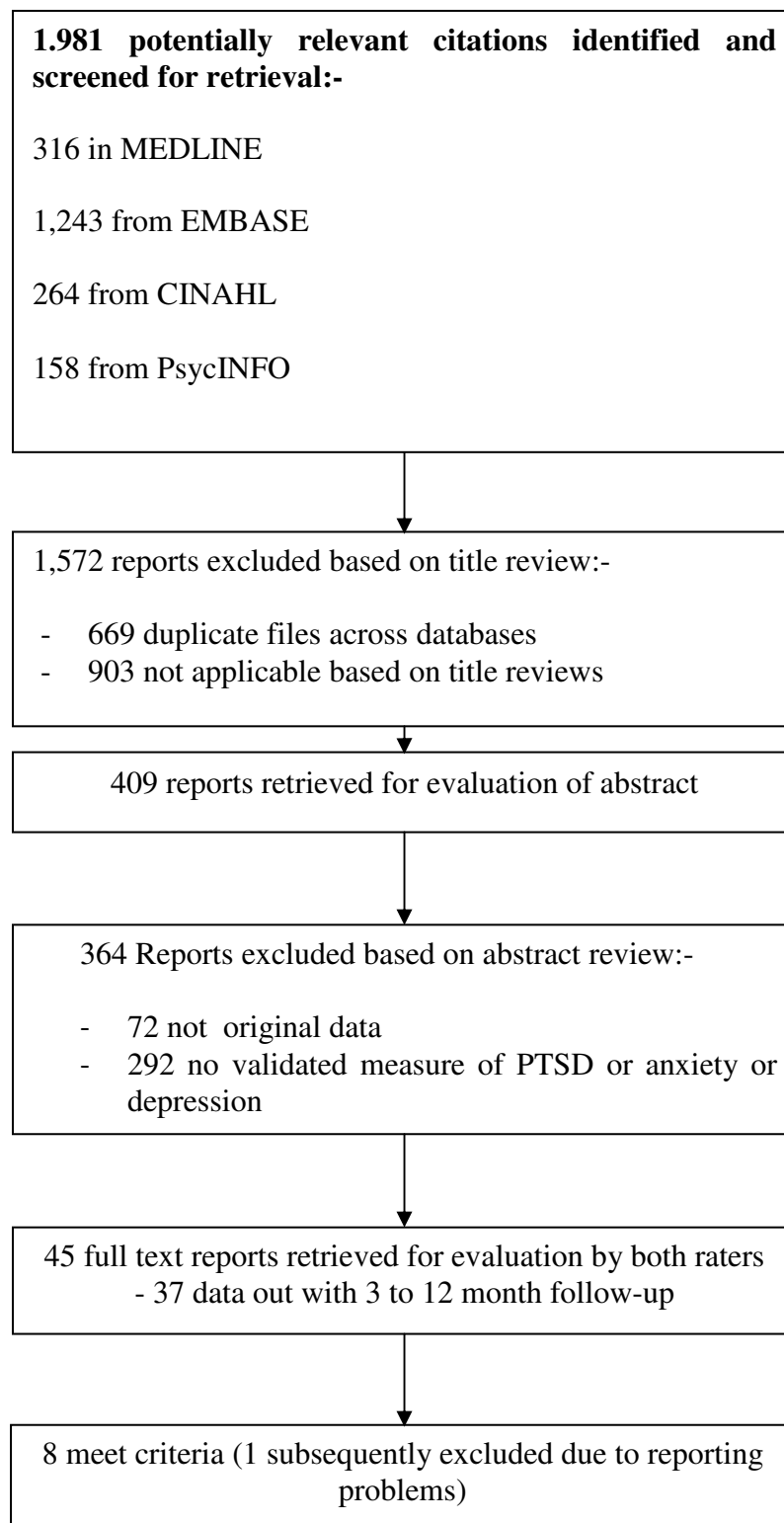


Fig. 3.1 Flowchart of study selection

3.3.2 Study characteristics

All seven studies included recruited participants from general ICUs, although there was substantial heterogeneity in the clinical presentation of participants (Table 3.1). Three of the included studies [26, 29, 32] were particularly poor in terms of identifying the sample, merely stating the participants were recruited from general ICU. Further heterogeneity was seen where, two studies excluded patients with pre-ICU psychiatric illness [30, 32], whilst two studies only included patients who had been mechanically ventilated [29, 32]. Moreover, minimum length of stay varied with four studies insisting on at least 24 hours [27, 28, 29, 30], one 48 hours [32], one 72 hours [31] and one 96 hours [26]. Four studies were conducted in the UK [31, 32, 33, 34], one in Norway [30], one in Sweden [24], and one in France [27]. Four studies recruited from one site [26, 28, 30, 31]; one study recruited from three sites [32]; one study from six sites [29], and one from nineteen [27] sites. All of the lead hospitals for recruitment were university-affiliated, tertiary care centres in Western Europe. The RCT [32] reported that different recruitment rates at the three different sites were influenced by a number of factors including staff changes and resource constraint. Although all the studies recorded emotional distress measures at different time points, the studies' aims varied considerably. For example, four studies sought to determine the prevalence and risk factors for emotional distress [27, 28, 30, 31]; one study aimed to evaluate the effectiveness of a rehabilitation programme [32]; another study set out to assess patients' perceptions of ICU experiences and their effect on emotional distress [29]; and another study sought to describe a multi-disciplinary ICU follow-up system used to identify psychological distress [26].

Table 3.1 Characteristics of included studies

First author (pub, year)	Study Design	Setting	Inclusion (I)/ Exclusion (E)	N (% male)	Mean age (s.d.) <i>median (IQR)</i> [range]	Emotional distress Outcome Measures (cut-off)	Main Findings
Schandl (2011) [26]	Single centre cohort	General ICU	I: discharged between January & December 2007; 4 or more days in ICU ^c	48 (64%)	52.6(17.8)	HADS (cut-off ≥ 11) IES (cut-off ≥ 26)	No significant difference over time for IES or HADS-D, however a significant reduction HADS-A. 20 participants had isolated IES score over cut-off, 6 had HADS-A or HADS-D above cut-off, 8 had a clinically significant score in IES and HADS-A or HADS-D. Patients with high scores in IES and/or HADS-A or HADS-D at three months were younger than patients with low scores (age 46.3 ± 17 versus 57 ± 18 years, $p = 0.026$).
De Miranda (2011) [27]	Multi-centre cohort	100% COPD admitted to General ICU	I: COPD history; >24 hours in ICU E: inability to understand French; refusal to participate; mental incompetence	126 (% male UTD)	67(57-75)	HADS (cut-off ≥ 8) IES-R (cut-off ≥ 20)	Significant decrease in HADS-A and HADS-D from discharge to 3 months. Anxiety symptoms at 3 month more common for those with anxiety symptoms at discharge than other patients.

First author (pub, year)	Study Design	Setting	Inclusion (I)/ Exclusion (E)	N (% male)	Mean age (s.d.) <i>median (IQR)</i> [range]	Emotional distress Outcome Measures (cut-off)	Main Findings
Rattray (2005) [28]	Single centre cohort	General ICU: 27% gastrointestinal; 27% respiratory, 13% trauma, 11% vascular, 5% cardiac, 5% neurological, 12% other	I: all emergency admissions in ICU>24 hours; 18 years or over E: lived more than 100 miles from hospital	109 (60%)	54.5(17.6)	HADS (cut-off ≥ 8 borderline case; cut-off ≥ 11 definite case) IES (cut-off ≥ 20)	HADS-A and HADS-D significantly reduced between hospital discharge and 6 months, but no further reduction from 6 to 12 months. IES-A and IES-I scores did not significantly change over time. No difference between those interviewed at time 1 only and those interviewed at 6 months for IES-I, IES-A, HADS-A or HADS-D. Younger patients and women were more anxious.
Rattray (2010) [29]	Multi-centre cohort	General ICU	I: ICU stay of 24 hours or more; mechanically ventilated; 18 years or over E: head injured; following elective neurosurgery unable to give informed consent	118 (63% ;1 value missing)	60[17-84] one value missing	HADS ((cut-off ≥ 8 borderline case; cut-off ≥ 11 definite case) IES (0-8 low; 9-19 medium; ≥ 20 high levels of symptoms)	Anxiety, depression, avoidance and intrusion scores did not significantly reduce over time.

First author (pub, year)	Study Design	Setting	Inclusion (I)/ Exclusion (E)	N (% male)	Mean age (s.d.) <i>median (IQR)</i> [range]	Emotional distress Outcome Measures (cut-off)	Main Findings
Mhyren (2010) [30]	Single centre cohort	General ICU: Medical 24%; surgical without trauma (34%), physical trauma (34%)	I: 18-75 years; >24 hours in ICU E: language difficulties; major psychiatric illness (i.e. psychosis) ^a ; severe head injury; cognitive failure	255 (63%)	47.9(15.7)	HADS (cut-off ≥ 8 borderline case; cut-off ≥ 11 definite case) IES (cut-off ≥ 20)	No significant differences over time for HADS-A, HADS-D and IES. More surgical patients had a clinically significant depression score compared with medical and trauma patients. 35% of patients had persistent PTSD symptoms during follow up, whereas 38% never showed any sign of PTSD symptoms.
Sukantarat (2007) [31]	Cohort	General ICU major surgical operation 71% (abdominal 43%; cardiothoracic 20%, other 8%); acute medical emergency 39%	I: ICU length of stay ≥ 72 hours E: major medical or surgical therapy following discharge; could not be readily traced; lived at a distance; reluctant to undergo detailed testing	51 (43%)	57(14) 60(49,66) [27-82]	HADS (cut-off ≥ 10 for case anxiety; ≥ 8 for case depression) IES (avoidance sub-scale ≥ 21 ; intrusion sub-scale ≥ 18)	Internal correlations were reported between HADS-A and HADS-D ($p < .0001$ at each time point), between IES-I and IES-A ($p < .0001$) and between all four psychological parameters ($p < .002$ or greater). This study also reported that most cases of avoidance or intrusion were also cases of anxiety or depression.

First author (pub, year)	Study Design	Setting	Inclusion (I)/ Exclusion (E)	N (% male)	Mean age (s.d.) <i>median (IQR)</i> [range]	Emotional distress Outcome Measures (cut-off)	Main Findings
Jones (2003) [32]	Single centre cohort (as part of multi-centre RCT)	General ICU	I: ICU patient and ventilated E: ICU patient <48 hours; suffering from burn injury; unable to follow the manual or have language difficulties; neurosurgical patients; pre-existing psychotic illness; discharged for terminal care; unlikely to survive 6 month follow-up	69, 57 ^b (57%) ^b	59 (16)[17-84] ^b	SSTAI HADS (cut-off ≥ 11) IES (cut-off ≥ 20)	The focus of this study was the evaluation of a rehabilitation programme. IES scores were lower in the group receiving the treatment at 8 weeks.

^aReference to pre-existing or history of psychiatric illness ;^bControl group; ^cProtocol not followed as three patients with ICU stays shorter than 4 days were invited for follow-up due to perceived psychological problems in ICU; UTD= unable to determine; HADS= Hospital Anxiety and Depression Scale [15]; IES(-R)= Impact of Events Scale [33](Revised [34])

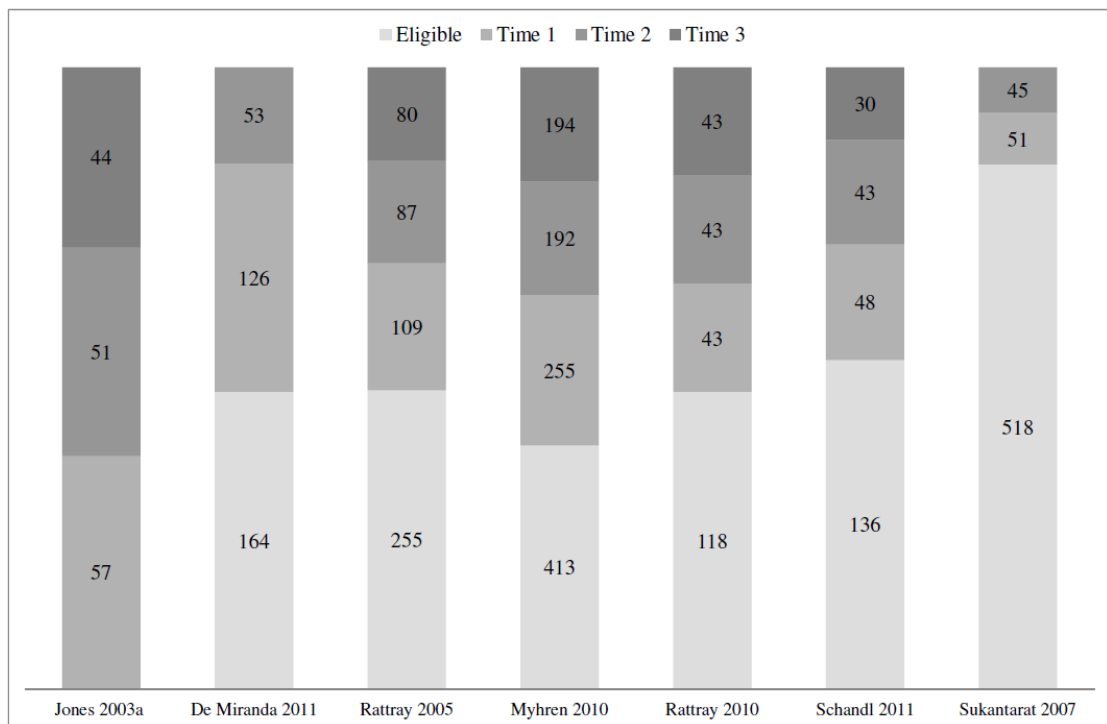
3.3.3 Attrition

The number of participants included in the studies varied from 48 to 255. Recruitment methods can be a potentially important source of bias and enrolling consecutive patients is the preferred method [19]. Five studies used this method [26, 27, 28, 29 and 30]. Figure 3.2 summarises the percentages of those eligible for uptake to the study and those participating over time. Sukantarat and colleagues [31] had a recruitment rate of 9.8% which was particularly poor, whereas the French study [27] was particularly strong recruitment rate of 76%. Of those recruited to each study the retention rate was particularly poor for this same French study [27] whereas Rattray and colleagues [29] reported 100% retention rate (which is very unusual in a longitudinal questionnaire based study). The studies which recruited from a six and 19 sites respectively [27, 29], no site level information was provided as to attrition rates which is poor.

Only two studies reported the demographics of those refusing to consent [28, 30]. It is extremely important in observational studies that readers are provided with some indication of representativeness of the sample to the general population and the majority of studies were unable to provide this. Of the two that did report the demographics, they were younger [28, 30], had a longer ICU stay [28], and were more often transferred to local hospitals while still on mechanical ventilation than the patients who participated at baseline (during hospital admission) [30]. Patients declining follow-up also had significantly higher scores predicting ten year mortality [30], lower education levels [30], were more likely to be unemployed [30] and had more co-morbid illness than those who came for follow-up (not statistically significant) [26]. It is unclear from the study [26] whether they had already signed up to the study or if this was prior to consenting; clarification was sought from the corresponding author of this study, however no reply was received. Myhren *et al* [30] provided the greatest information of demographics of those eligible to participate and those lost to follow-up.

In the largest study [30], data was reported on participants completing the questionnaires at 12 month follow-up only (but were not included in the analysis).

These participants were more often mechanically ventilated, had more nursing input during admission, and were more often within the subset of patients admitted to general ICU for physical trauma compared with participants who completed at one month [30]. This study also looked at precipitating factors and found those lost to follow-up had lower educational status and were more often unemployed before ICU stay compared with those who completed the study at 12 months but did not differ in clinical characteristics [30].



a No information provided for eligible participants and controls group presented in graph

Fig. 3.2 Graph of those eligible to participate and those who participated at follow-up points.

Two studies compared psychological characteristics of those lost to follow-up with those completing the study [28, 30]; one found no significant differences in PTSD avoidance or intrusion symptom sub-scale scores at discharge or six months later (total PTSD symptom scores were not reported) [28]. Another study found no significant difference between completers and those who dropped out on PTSD total scores [30]. Moreover, no differences in anxiety or depression were observed between these groups [28]. The largest study [30] highlighted that those lost to

follow-up were more anxious at baseline than those who completed. This is inconsistent with Rattray *et al* [28] findings which state no evidence of withdrawal bias with regards to outcome measure results. One study [30] also compared the subgroup that completed at twelve months but not at three months (n=27) and found that those that did not respond at three months had significantly higher IES total mean score at twelve months compared with patients who answered at all three time points. This study [30] also found that those lost to attrition at three months did not significantly differ in anxiety or depression scores. Again, the Norwegian study [30] provided the most robust information on emotional outcomes of those eligible but did not participate and those lost to follow-up which is extremely important to identify representativeness and the potential for selection bias.

3.3.4 Outcome measures

Self-report questionnaires were used in all studies to measure levels of emotional distress. The Impact of Events Scale (IES) [33] or the Impact of Events-Scale Revised (IES-R) [34] was used to evaluate PTSD symptoms. The HADS [15] was used in all studies to measure symptoms of anxiety and depression. One study administered the questionnaire over the phone [27]; four in-person [26, 28, 31, 32], and two posted out questionnaires [29, 30]. Notably, not all of the studies used the same cut-off score for specific levels of emotional distress (see Table 3.1). Sukantarat *et al.* [31] reported intrusion and avoidance subscale scores, however not total scores which meant that the course of PTSD could not be identified over time.

The means over time, standard deviation and absolute number of people meeting caseness is described in Table E3.1.

Supplementary Table E3.1² Characteristics of included studies

Months	Anxiety				Depression				PTSD			
	0	3	6	12	0	3	6	12	0	3	6	12
Mean Score	7.23	5.44	6.66	5.82	6.30	6.10	5.95	4.96	UN	21.9 1	13.8 7	23.6 0
SD	4.83	4.60	3.55	4.47	4.22	4.38	4.21	4.20	UN	16.9 5	12.8 5	17.1 4
Total No. meeting caseness*	40/ 243	21/ 44	10/ 45	42/ 237	38/ 166	37/ 296	18/ 174	23/ 194	UN	55/ 243	18/ 44	52/ 194
No studies	2	3	3	3	2	2	3	3	0	3	2	2

UN is data unavailable; * caseness refers to HADS Anxiety ≥ 11 ; HADS Depression ≥ 11 ; IES-R ≥ 33 ;

From the data available to the authors, the mean percentage of clinical caseness for anxiety, depression and PTSD over time was calculated as well as the respective linear trends from the data available and reported in Figure 3.3 with the longitudinal course of PTSD following rape [17] for comparison. There was no significant change in PTSD symptoms [26, 28, 29, 30, 31]; depression or anxiety scores [26, 29, 30, 31] over time in the majority of studies. Two studies did note a reduction in anxiety scores [27, 28]. However the tests of overall mean values hide individual difference profiles, so although overall there is little shift in average group scores, changes appear to occur at the intra-individual level. For example, the largest study reported the course for individuals over time, where 33% demonstrated persistent PTSD symptoms, 38% never met threshold for PTSD and 16% of individual's scores increased over the 12 month follow-up [30].

² This table is to be included in supplementary material for journal purposes

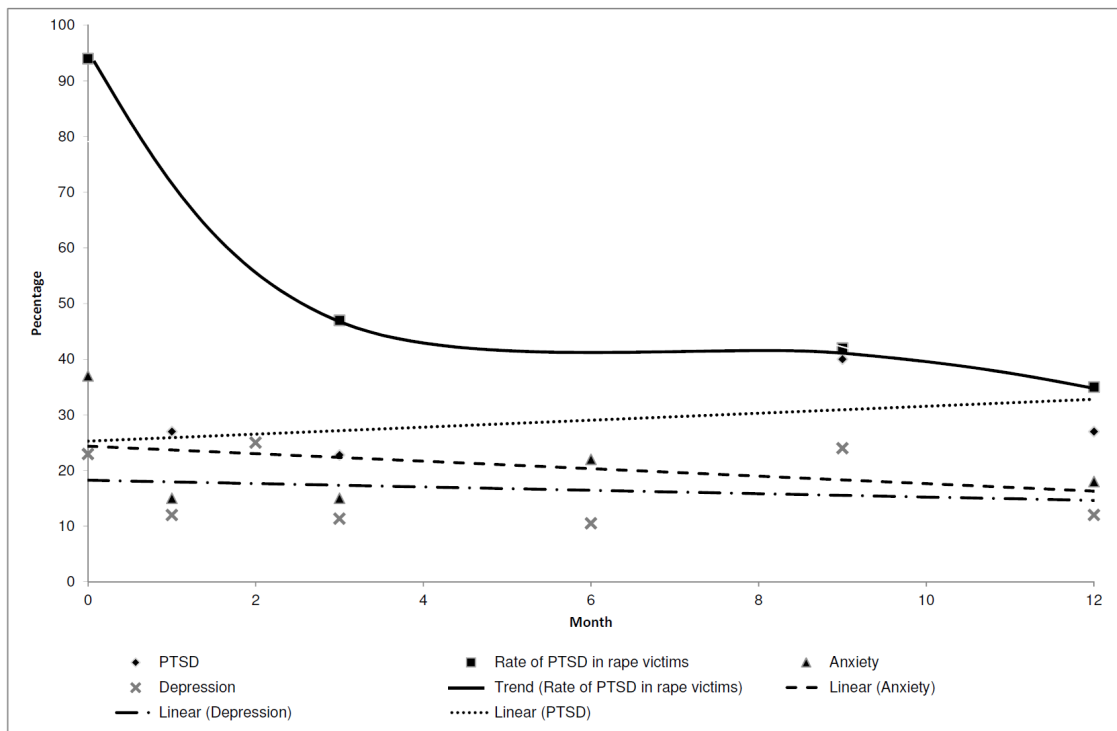


Fig 3.3 Mean clinical caseness (and linear trend) for post ICU anxiety, depression and PTSD plotted against clinical rate of change of PTSD symptoms in rape victims

3.3.5 Missing data

Two studies stated how incomplete data was managed [29, 30] - for all other studies it was impossible to determine how the missing data was dealt with. Given the high rates of attrition, particularly in the French study [27] it is unclear whether attrition bias was observed as missing data was not described.

3.3.6 Reporting quality of studies included

The reporting quality of the included studies is reported in Table 3.2. The intra-class coefficient was Cronbach's alpha of 0.919 for the reporting quality of raters AK and KYM. Areas of weakness for all studies included explaining why a study size was used and the potential for bias in the study results. The relative strengths of these papers were that specific objectives were defined, details of the eligibility criteria was highlighted as well as sources of participants and methods of selection of participants were reported. However, it must be highlighted that although the papers scored high in reporting criteria this does not mean that this is a low susceptibility to bias.

Table 3.2 Assessment of reporting quality (STROBE 1-22)

First author (pub, year)	Title	Background	Objectives	Design	Setting	Participants	Variables	Data sources	Bias	Study size	Quantitative variables	Statistical methods	Participants	Descriptive data	Outcome data	Main results	Other analyses	Key results ⁸	Limitations	Interpretation	Generalisability	Funding
Jones (2003)	*	*	*	*		*	*	*	*	*	*	*	*	*	*		*	*	*	*	*	*
De Miranda (2011)	*	*	*	*			*	*			*	*	*	*	*	*		*	*	*	*	*
Rattray (2005)	*	*	*	*	*	*	*	*	*		*	*	*	*	*	*	*	*		*	*	*
Mhyren (2010)	*	*	*	*	*	*	*	*	*		*	*	*	*	*	*	*	*	*	*		*
Rattray (2010)	*	*	*	*	*	*		*			*	*	*	*	*		*	*	*	*	*	*
Schandl (2011)	*	*		*	*		*	*			*	*	*	*	*	*		*				*
Sukantarat (2007)	*	*		*	*	*	*	*			*	*	*	*	*			*	*			*
TOTAL	7	7	5	7	5	5	6	7	3	1	7	7	7	7	7	4	4	7	5	5	4	7

The description of each item is as follows is in Appendix 3

3.4. Discussion

3.4.1 Overview

Our findings suggest that one month following discharge from hospital, ICU survivors commonly experience clinically significant levels of anxiety; depression, and PTSD symptoms and it appears likely that these rates change little over the subsequent eleven months. Although existing studies are heterogeneous and differ in important ways, the evidence indicates that about one in six survivors report significant levels of anxiety; about one in eight significant levels of depression and about one in four have clinically meaningful levels of PTSD symptoms over the first year of recovery. There is some evidence (from two studies) that at discharge, nearly one in four ICU survivors may be experiencing clinical levels of anxiety but this seems to have resolved for many one month later. The prevalence of anxiety and depression 12 months after leaving hospital is about twice that found in the general population (7% and 5%, respectively). The levels of PTSD co-morbidity appear to be considerably lower (about 40%) in ICU than is generally found to be the case (about 80%) in the general trauma literature [12].

The numbers of people with clinically significant levels of PTSD symptoms do not attenuate over time, which usually occurs following traumatic events. For example, epidemiological studies of trauma in various populations show rates of 47% and 23% at 3 months and 37% and 16% twelve months later for rape and road traffic accidents respectively [17, 35³]. Unfortunately the two studies that collated PTSD scores at baseline only reported levels of intrusion and avoidance symptoms and not total scores.

3.4.2 Strengths and limitations of review

The study samples were heterogeneous in many ways which, whilst consistent with previous reviews in this clinical area, could impact on results. Most studies were conducted at university teaching hospitals and all were within Europe. However, the extent to which these healthcare organisations were similar and dissimilar is unclear and of course it is uncertain whether or not these findings can be generalised to non-

³ From personal communication (1 July 2012) with the Journal of Critical Care, exceptions can be made to the maximum number of references in review papers (e.g. Nouwen *et al*, 2012)

teaching hospitals and other parts of the world. The fact that across studies differences were evident in the average age of participants; percentages of males participating; overall uptake rate from potential participant pool, and clinical presentations included may account for a degree of the variability in results. Exclusion of pre-ICU psychiatric illness criterion in some studies would likely have led to conservative estimates of significant emotional distress, partly because previous mental health problems is a well recognised vulnerability factor in the development of PTSD symptoms following traumatic events [12]. Many studies reviewed did not explore potential differences between those who completed the study and those who were lost to attrition. Of those that did, lower education levels and being unemployed were notably more common among non-completers [30]. Again, this is important because both of these factors frequently co-occur and are associated with higher rates of mental health problems [14].

Clearly, the reliability and validity of outcome measures are crucial. All review studies used the HADS to measure anxiety and depression symptoms. This is an extremely well-researched measure [16] and is commonly used clinically and in research on adults who have physical health problems. Although the HADS is recommended for use in ICU settings [36], it has not been validated with ICU populations. There are potential confounding items - for example, a participant's response to "I feel as if I am slowed down" may be due to symptoms of depression but similarly be influenced by medication or physical limitations of conditions. On the other hand, the HADS has been validated for use with many different medical conditions [16] and this kind of symptom overlap would commonly occur. The majority of papers used the IES to assess PTSD symptoms. The IES measure is limited in that it does not measure hyper-arousal which is a core facet of PTSD [13], however it is a widely used inventory and like the HADS has been extensively researched and deployed. Little is known about the pre-ICU psychological health of study participants. We do know that chronic ill-health is associated with substantially higher levels of anxiety and depression than occurs in the general population [37], so any pre-existing medical conditions could be influential in study results. Moreover, an earlier systematic review [10] identified pre-ICU emotional distress as a

significant risk for post-ICU distress as well as post-ICU memories of frightening or psychotic experiences during patients' time in ICU. This review did not find female sex, duration of mechanical ventilation, ICU length of stay or relative youth to be consistent predictors, whereas female sex, younger age and pre-existing psychological distress have been identified as key vulnerability factors for distress in the general trauma literature [14]. However, this review this is consistent with a previous review [10] looking at PTSD post-ICU which found female sex and younger age to be less consistent predictors but that review [10] also had many limitations similar to our review, such as heterogeneity of clinical presentations.

Over half of the studies in this review were published in the last two years suggesting an increased awareness and research focus of the psychological outcomes following ICU admission. Our findings indicate lower prevalence rates than older systematic reviews within ICU [9, 10]. Our presentation of results attempts to highlight the general trend of clinical caseness over time in order to improve on previous reporting of median point prevalence rates. Median point prevalence rates do not allow separation of participants between those who do and do not report clinically significant levels of psychological problems, and this is important to clinicians and health care managers, alike. We have also deliberately used standard clinical cut-off values on the HADS of ≥ 11 to try to avoid the possibility of inflated rates of anxiety and depression (previous reviews used the borderline-clinical levels of ≥ 8).

The fact that different studies used dissimilar cut-off points to indicate clinical levels of psychological problems is unsatisfactory (some data could not be used in results), but nevertheless the results of the seven studies were broadly in keeping with one another. The studies reviewed used the same measures which helped illuminate findings as it is commonly highlighted in systematic reviews of psychological topics that the array of different measures used causes problems when comparing results in a meaningful way.

3.4.3 Implications for current practice and future research

Recent critical care guidelines [4] (derived mostly from clinical opinion due to the scarcity of research) recommend that psychological screening should be carried out during admission to ICU and at two to three months follow-up. Evidence herein indicates that this would likely be helpful, not only because it is important that health care systems consider physical and psychological wellbeing, but also because they are naturally entwined [37]. For example, it is well documented that when someone experiences clinical levels of emotional distress, they may be more likely to miss hospital appointments; struggle to cope with any physical impairment; find it difficult to adhere to rehabilitation and self-management regimens, and become less engaged in life in general [38]. Therefore, early identification would be prudent to increase chances of physical recovery; improve overall quality of life, and reduce health care need. In the United Kingdom, clinical guidelines [4] recommend post-discharge care pathways and this approach would appear sensible in view of the lasting psychological difficulties identified.

There is a clear need for multi-centre observational studies involving large numbers of participants with longer follow-up periods. This is required both for ICU survivors as a whole and also for sub-groups.

Exploration of potentially important factors before; around, and after ICU admission may yield clinically useful information and help health care systems target especially vulnerable groups and identify risk and protective factors. Importantly, it appears that the majority of people admitted to ICU do not suffer significant psychological problems. This resilience has similarly been recognised in the general trauma literature and has led to substantial interest in the concept of post traumatic growth (positive changes that occur following traumatic experiences) [39].

3.4.4 Conclusions

There appears to be elevated levels of psychological problems among ICU survivors. Unusually, PTSD symptoms do not seem to attenuate over time and the reason for this is currently unclear. Existing literature has limitations but there are indications of

a growing interest in the psychological wellbeing of ICU survivors post-discharge. Larger, multi-centre, higher quality studies are required and a robust, widely-accepted methodology for assessing the quality of observational studies would be helpful. At our current levels of understanding, it is evident that ICU survivors require psychological care as well as physical rehabilitation. It is likely the two are intimately entwined and health providers should consider carefully the need for appropriate systems of care to meet ICU survivors' needs.

3.5 References

* indicates studies included in review

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4. BRIDGING CHAPTER

4.1 Intensive care and psychological outcomes

Every year a significant number of people in the United Kingdom require admission to intensive care for the treatment of life-threatening illness (National Institute of Health and Clinical Excellence (NICE), 2009). Due to the advances in critical care medicine within ICU settings, an increasing number are surviving a life-threatening illness (Angus & Cartlet, 2003). As a consequence, the focus of research has shifted from mortality rates to longer-term patient outcomes, both physical and psychological.

Research in the field has demonstrated that ICU survivors report poorer quality of life compared to the general population (Dowdy *et al.*, 2005; Myhren *et al.*, 2010). Furthermore, as detailed in the preceding systematic review (Matheson, unpublished), patients surviving critical illness have been found to have persistent levels of emotional distress one to twelve months post ICU discharge. Although it can be helpful to identify specific psychological disorders such as post-traumatic stress disorder (PTSD) and depression in isolation, it is also important to look at emotional outcomes in a broader sense as, for example, it is argued that PTSD has a multi-factorial aetiology and multi-dimensional presentation (Brewin *et al.*, 2000).

What remains unclear is if ICU admission itself is an independent risk factor for psychological distress or whether other variables (including pre-existing emotional distress, the lasting effects of medical conditions themselves, treatments and/or physical recovery processes) confound post ICU psychological outcomes. While a history of mental health problems prior to critical illness could be the primary risk factor for post-ICU emotional distress, few studies have examined prior psychological disorders as potential risk factors (Davydow *et al.*, 2008; 2009). There is limited research reporting pre-existing psychological distress for PTSD in general (NICE, 2005).

Intensive Care Unit (ICU) admission for the treatment of critical illness is an issue of particular importance in Scotland for those with chronic health conditions as they

account for approximately one in five admissions (Scottish Intensive Care Society Audit Group, 2011). One of the most prevalent long term conditions in Scotland is diabetes with 247,278 living with a diagnosis of the condition in 2011 (Scottish Government, 2012). A recent national diabetes survey has highlighted that over £301 million per year is spent providing inpatient care in Scotland for people with diabetes (Scottish Government, 2012). Reducing the number of diabetes emergencies (which are a financial burden on the NHS) is a national action point. Two major causes of emergency situations for people with diabetes are hypoglycaemia and diabetic ketoacidosis which are experienced by both people with Type 1 and Type 2 diabetes.

4.2 Diabetes

4.2.1 Type 1 diabetes

Approximately 3,042 people are known to have Type 1 diabetes in National Health Service (NHS) Grampian. The prevalence rate has been steadily rising over recent years and in 2010 over 28, 272 people in Scotland had a diagnosis of this long term medical condition (Scottish Government, 2012).

Type 1 diabetes arises when the pancreas is no longer able to produce insulin because the beta cells that do this have been destroyed by the body's immune system. Insulin is the hormone that is fundamental to the process of turning glucose in the blood (obtained through consuming carbohydrates) into stored energy; hence when there is an insulin deficit this leads to an increase in glucose levels in the blood. Type 1 diabetes is most commonly identified in children and young adults. About 11.4% of those with diabetes have Type 1 diabetes.

4.2.2 Self-management in Type 1 diabetes

Before the discovery of insulin in the 1920s, most people who developed Type 1 diabetes died within 12 months. In order to survive, people with Type 1 diabetes need to administer daily injections of insulin. In addition to this, to prevent acute complications, people with Type 1 diabetes need to maintain their blood glucose levels within certain limits, which require continual adjustments to their insulin regimen and various areas of life such as diet and exercise levels. These adjustments

to medications and fundamental aspects of life are typically referred to using the term “self-care” or “self-management”. Health professionals describe the outcome of efforts to self-care as “diabetes control” which is frequently measured by haemoglobin (HbA_{1c}). This is a form of glycaeted haemoglobin and is the standard measure of blood glucose control over the preceding three month period. In the short term if adequate control is not achieved, then blood sugar levels will become either too high (hyperglycaemia) or too low (hypoglycaemia) and both can lead to coma and death. In Scotland, most people with diabetes do not attain good control (Short Life Working Group on Type 1 Diabetes, 2009). Although there is no evidence on exactly what average blood glucose level is required to minimise the probability of long-term diabetes-related complications, there is an abundance of evidence showing that lower HbA_{1c} values lead to better health outcomes – for example, the Scottish Intercollegiate Guideline Network (SIGN) 116 guidelines recommend an HbA_{1c} of approximately 7% (53mmol/mol) to minimise the risk of onset and progression of diabetes-related eye disease.

4.2.3 Emotional distress and diabetes

Barriers for people to effectively manage their diabetes vary. Many of the difficulties people experience when trying to improve their diabetes control relate to how they think about themselves, their beliefs about their condition and to their emotional wellbeing in general. Typically, these factors are related. For example, meta-analyses have indicated that depressive and anxiety symptoms are associated with poorer blood glucose control (Lustman *et al.*, 2000; de Groot *et al.*, 2001; Anderson *et al.*, 2002). However, identifying depression and anxiety in people with diabetes is notoriously difficult due to symptom overlap with diabetes (CMO Psychology Advisory Committee, 2003). For example the physiological features of depression (such as increased sympathetic activity) may contribute directly to hyperglycaemia associated with Type 1 diabetes (Musselman *et al.*, 2003). This is of considerable importance because the prevalence of depression among people with diabetes is about 10 to 20% (Anderson *et al.*, 2001) and that of anxiety ranges from 14 to 49% (Grigsby *et al.*, 2002).

4.3 Diabetic ketoacidosis

4.3.1 Diabetic ketoacidosis

The most dangerous complication of Type 1 diabetes is diabetic ketoacidosis (DKA) which is characterised by hyperglycaemia, acidosis and ketonaemia. Common presenting symptoms are vomiting, dehydration, hyperventilation and drowsiness. Its underlying causes include substantial and enduring difficulties around self management, and acute infection. DKA is a critical life-threatening condition and in the United Kingdom those with DKA are frequently admitted to ICUs in line with the nationally agreed protocol (NHS Diabetes, 2010).

DKA is treated using a combination of frequent insulin injections, rehydration by intra-venous tools, replacing any minerals and in those who are unconscious. A feeding tube can be used to remove stomach contents in order to prevent people breathing in vomit.

4.3.2 Complications of diabetic ketoacidosis

A number of serious complications of DKA can occur, including acute kidney failure, cerebral oedema, and adult respiratory distress syndrome. Mortality in the United Kingdom from DKA is low at approximately 2% (Wright *et al.*, 2009), however, this increases in those aged over 30 years (Skriverhaug *et al.*, 2006), in recurrent admissions, clinic non-attendance, with alcohol abuse and poor glycaemic control (Wright *et al.*, 2009). In both males and females, incidence of DKA and mortality are also associated with psychosocial problems (Wright *et al.*, 2009). Risk factors for admission with DKA include psychological problems and lower socio-economic status (Wright *et al.*, 2009). However death from DKA is potentially avoidable as the condition is largely preventable if patient education and access to care are adequate (Kitabachi *et al.*, 2009).

4.3.3 Ketones

Providing there are no complications, patients should be able to leave hospital when they are well enough to eat and drink normally and they have no or very small amounts of ketones left in their body (typically 24-48 hours) (NHS Diabetes, 2010).

Ketones are acidic compounds remaining when the body burns its own fat. When the body has insufficient insulin, it cannot get glucose from the blood into the body's cells to use as energy and will instead begin to burn fat. In Type 1 diabetes high blood sugar levels can produce ketones. Ketones are dangerous at high levels, and are those with Type 1 diabetes are at risk of ketoacidosis when blood glucose levels become too high.

4.3.4 Clinical management of diabetic ketoacidosis

As per the Joint British Diabetes Societies guideline for the management of DKA (Savage *et al.*, 2011), the Diabetes Specialist Inpatient Team must always be involved in the care of those admitted with DKA. Their role is assessment of precipitating factors, management, discharge, provision of self-management tools (e.g. ketone meters) and follow-up (including assessment of the patient's understanding of diabetes, their attitudes and beliefs).

4.4 Summary

It is apparent that admission to ICU is increasingly important in Scotland and in particular for those with long term conditions which account for one in five ICU hospital admissions. One of the most prevalent chronic conditions in Scotland is Type 1 diabetes. Overall, there is reasonable evidence, that there is considerable interplay between diabetes control and emotional wellbeing and based on the previous systematic review (Matheson, unpublished) there is evidence of increased psychological problems among those discharged from ICU with non-diabetes related conditions. As far as the authors' are aware, there is no existing literature on the psychological outcomes among adults with diabetes following admission for DKA. The primary aim of this study therefore is to investigate the symptoms of PTSD; anxiety, and depression among adults with Type 1 diabetes who have been discharged from ICU having been successfully treated for DKA.

5. METHODOLOGY

Overview

This study investigated the emotional distress of patients following admission for diabetic ketoacidosis (DKA).

5.1 Design

This study is a prospective longitudinal cohort study.

5.2 Participants

The sample comprised people with Type 1 diabetes who had been admitted to Aberdeen Royal Infirmary (ARI) for the primary reason of DKA between 1st September 2011 and 31st March 2012. The diagnosis of DKA was made by the inpatient diabetes team.

5.3 Inclusion and exclusion criteria

5.3.1 Inclusion criteria

All participants were required to have:-

- A diagnosis of DKA (Ketonaemia 3 mmol/l and over or significant ketonuria, and blood glucose over 11 mmol/l or known diabetes mellitus and HCO₃ below 15 mmol/l and/or venous pH less than 7.3) as defined by National Health Service (NHS) Diabetes (2010).
- A pre-existing diagnosis of Type 1 diabetes prior to admission to tertiary care (that is, they were not admitted immediately following (probable) diagnosis in general practice or elsewhere).
- The capacity to consent to the study (this decision was made by the consultant diabetologists).
- Had their acidosis corrected and be eating and drinking (these judgements were made by the inpatient diabetes team).
- Been fluent in the English language.

5.3.2 Exclusion criteria

There were no criteria other than not meeting the inclusion criteria.

5.4 Procedure

5.4.1 Recruitment procedure

All potential participants were approached by a senior member of the diabetes inpatient medical team and asked if they wished to be approached about taking part in this study (agreed with the NHS North of Scotland Ethics Committee; approval Appendix 5). If they agreed, the author was contacted and attended the ward to explain to the potential participant what the project entailed and answer any questions. An information sheet (Appendix 6) was also provided for potential participants to read. Potential participants who continued to express an interest in taking part were then presented with a consent form to sign (Appendix 7). A diagrammatic representation of the sequence of events leading to participants providing consent is presented in Figure 5.1.

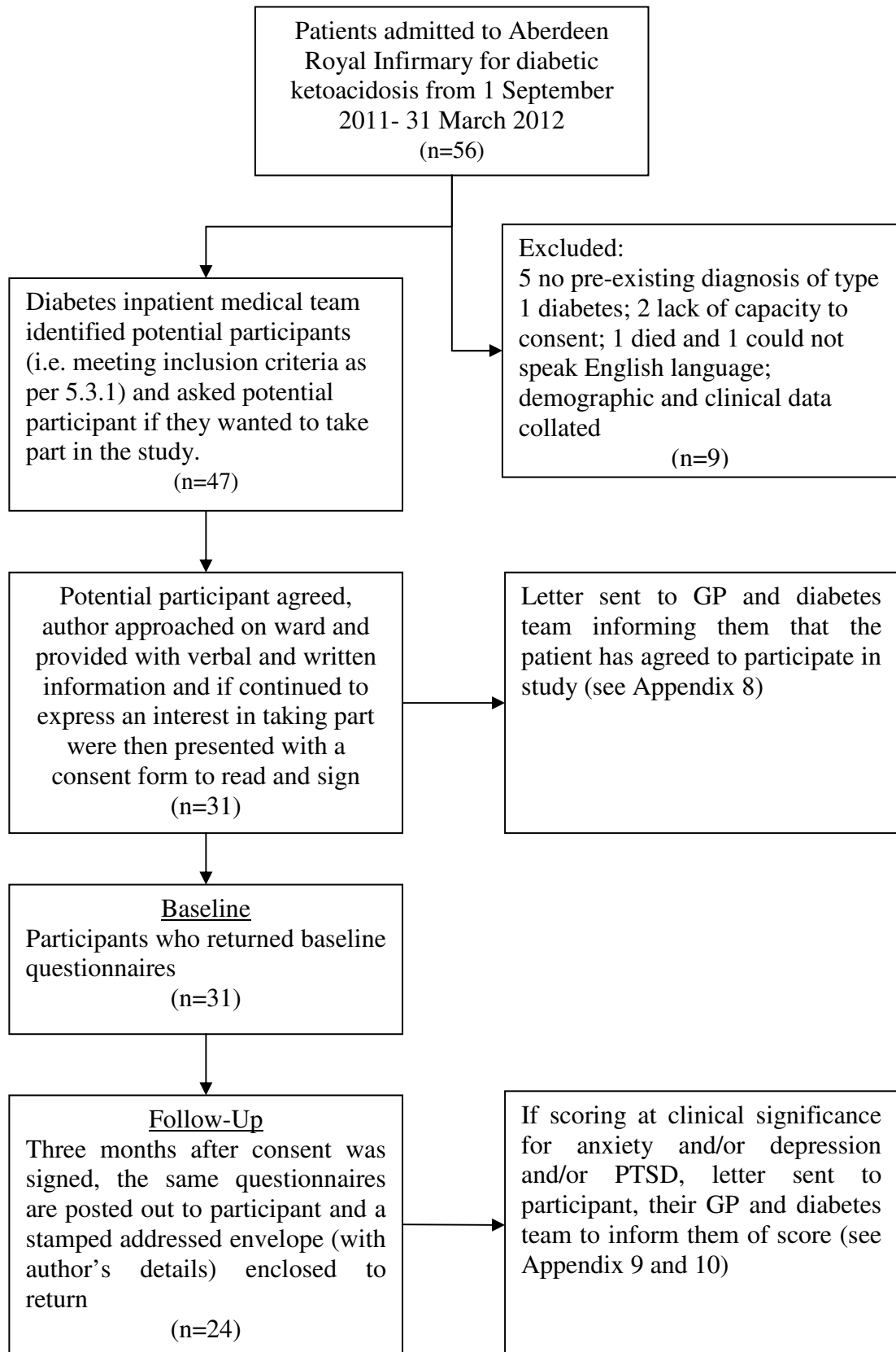
5.4.2 Assessment procedure

All participants were given three questionnaires at two time points - during admission to ARI for DKA (baseline) and three months post-discharge (follow-up). The measures used are described below (section 5.5). 66% of eligible participants completed all inventories at baseline. 77% of those who completed the questionnaires at baseline also returned all inventories at three month follow-up (therefore 51% of those eligible completed the inventories at both time points). A diagrammatic representation of the recruitment and assessment timeline is presented in Figure 5.1.

5.5 Measures

As indicated previously, a total of three measures were used and these are discussed in following sections (5.5.3 to 5.5.5). A description of the medical and demographic data collected is also provided.

Figure 5.1: Recruitment and assessment time line:-



5.5.1 Demographic & pre-existing clinical information

Demographic data (sex, age) and clinical data (duration of diabetes, previous DKA; number of contacts with Diabetes team in year preceding DKA; precipitant to DKA; length of hospital stay; pre-existing levels of anxiety and depression) were obtained from medical records and SCI-DC Network (a national diabetes database) and provided information of participants' clinical presentation and histories.

The Scottish Index of Multiple Deprivation (SIMD) quintiles were used to describe the relative deprivation of those admitted for DKA, with group 1 being the most deprived and group 5 being the least deprived.

5.5.2 Diabetes control

Diabetes control (HbA_{1c}) is the internationally recognised standard measure of glycaemic control and is the most often cited as the most reliable, long term indicator of risk of long term complications among people with Type 1 diabetes (World Health Organisation (WHO), 2011; Scottish Intercollegiate Guidelines Network (SIGN), 2010). Diabetes control provides an indication of average diabetes control over approximately the previous three months. An indication of pre-existing glycaemic control was obtained by obtaining the most recent HbA_{1c} reading (prior to hospital admission). The date of this reading was also recorded. Similarly, post-discharge HbA_{1c} values were obtained for participants in order to ascertain glycaemic control following hospitalisation (only values which were collected at least three months post-discharge were documented as values collected before this time would be skewed due to the high levels of blood sugar levels during the DKA event). The overall mean and standard deviation of HbA_{1c} for adults with Type 1 diabetes in Grampian (N= 2968; excluding the DKA study sample) was calculated using data obtained from SCI-DC Network (a national diabetes database used in routine clinical practice across primary and secondary care in Scotland). The purpose of this was to decipher whether this study's sample was representative, in terms of diabetes control of the overall Type 1 diabetes clinic in National Health Service (NHS) Grampian.

5.5.3 The Hospital Anxiety and Depression Scale

Description of the Scale

The Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) was used as a brief screening tool for anxiety and depression. It is short (14 items) and controls for the overlap between somatic symptoms of medical conditions and the somatic symptoms of anxiety and depression. The scale is divided into two scales (anxiety and depression), both of which contain seven items. Respondents are required to consider each item in relation to the extent to which they have felt this way during the past week and to specify their response on a four point Likert scale. Each of the items is on a scale from 0 to 3 with three indicating the highest symptom severity and a total score for each subscale is derived by summing all the item scores for that sub-scale. The scores on the HADS can be separated into three categories, whereby a total score on each subscale defines the category. A subscale score of 0 to 7 indicates 'Normal' (referred to as non-case), a subscale score of 8 to 10 is defined as 'Mild' (referred to as borderline-case) and a score of 11 or greater indicates 'Severe' (referred to as case) (Zigmond & Snaith, 1983). The cut-off of 11 or more is used in this study to define clinical caseness. A copy of the HADS is presented in Appendix 11.

Psychometric Properties of the HADS

Each subscale of the HADS is reported to have high internal consistency, with correlation coefficients ranging between $r=.80$ and $r=.93$ for the anxiety subscale and $r=.81$ and $r=.90$ for the depression subscale (Herrmann, 1997). In a comprehensive review of 747 articles, Bjelland *et al.* (2002) demonstrated that the HADS has good external validity. Zigmond and Snaith (1983) reported that the HADS can reliably detect anxiety and depression and perform well in assessing symptom severity. The HADS is the most widely used self report screening tool for anxiety and depression in adults with medical conditions, including diabetes in the UK (Scottish Intercollegiate Guidelines Network, 2010). Some of the reasons for the high usage include: it is brief and simple to administer, it appears to separate anxiety from depression and it is not confounded by physical illness to the same extent as measures that include many items tapping somatic symptoms (McDowell, 2006).

Although there is no good quality evidence ascertaining the validity and reliability in those with Type 1 diabetes, the use of the HADS with adults who have diabetes in Scotland was recommended by an expert panel (Psychology Working Group, 2006).

5.5.4 Impact of Events Scale - Revised

Description of the Scale

The Impact of Events Scale-Revised (IES-R; Weiss & Marmar, 1997) is a 22-item self-report scale assessing subjective distress after a stressful life event. The IES-R outlines eight items relating to experience of traumatic intrusions (such as thoughts, feelings or images of the event), eight items pertaining to experiencing avoidance (such as trying to avoid reminders of the trauma or dulling their emotional reactions to it) and six items related to hyperarousal symptoms (such as feeling irritable or being easily startled). Participants are asked to rate the degree of distress caused by each item within the past seven days on a four-point scale (scoring 0 if an item is not distressing at all, to scoring 4 if the item has been extremely distressing). Participants' ratings generate a total IES-R score (the sum of the subscale scores). A cut-off of 33 has been cited to provide the best diagnostic accuracy (Creamer *et al.*, 2003) and was applied in this study. A copy of the IES-R is presented in Appendix 12.

Psychometric Properties of the IES-R

The IES-R is a modified version of the Impact of Events scale (IES; Horowitz *et al.*, 1979) which did not include the subset of hyperarousal and a question about flashbacks. Weiss and Marmar (1997) intended the IES-R to be comparable with the original scale, adding to most of the original questions. The IES specifically is considered a reliable tool, with high internal consistency (reflected in Cronbach's alpha ranging from .87 to .91 for intrusions, .84 to .85 for avoidance and .79 to .9 for hyperarousal) (Sundin & Horowitz, 2002). The IES-R measure has demonstrated reliability within a variety of trauma-exposed populations, including burns and cardiac events (Sveen *et al.*, 2010; Baumert *et al.*, 2004). Studies examining the factor structure of the IES-R have found different factor solutions varying from one to five factor solutions (Asukai *et al.*, 2002; Baumert *et al.*, 2004; Beck *et al.*, 2008;

Creamer *et al.*, 2003; Morina *et al.*, 2010). Creamer *et al.* (2003) report that a total score of 33 on the IES-R yields diagnostic sensitivity of .91 and specificity of .82.

The IES-R is recommended as a self-report measure for post traumatic stress disorder symptoms (National Institute of Clinical Excellence (NICE), 2005). To date, the IES has been used in a number of prospective studies investigating PTSD symptoms following admission for a medical emergency, such as severe critical illness, severe trauma and chronic obstructive pulmonary disease (Jones *et al.*, 2001; Tøien *et al.*, 2010; de Miranda *et al.*, 2011). Although there is no good quality evidence establishing reliability and validity of the IES-R in those with acute complications of Type 1 diabetes, it was highlighted by D. Weiss (personal communication, 14 June 2011) that the closer the medical event is to unexpected threat of death, the more appropriate is the IES-R. Though many have used the measure in the context of receiving a diagnosis of a potentially fatal illness, the re-living experience is different from being actually threatened with death. In these circumstances the intrusion and re-experiencing is not of a possibility in the future, but of an actuality that has passed (D. Weiss, personal communication, 14 June 2011).

5.5.5 Problem Areas in Diabetes

Description of Scale

The Problem Areas in Diabetes (PAID; Polonsky *et al.*, 1995) is a screening tool used to identify diabetes related distress. It is a 20-item scale that describes common problematic situations for people with diabetes, each representing a unique area of diabetes-specific emotional distress (Polonsky *et al.*, 1995; Polonsky & Welch, 1996). The self-report questionnaire is rated on a four-point Likert scale. Each item is scored one to four (1 is "not a problem" to 4 a "serious problem"). The sum of the 20 items is multiplied by 1.25 to yield a final score from 0 to 100. A higher score represents greater diabetes related distress. Examples of items in the PAID include, "not accepting your diabetes?" and "feeling that your friends and family are not supportive of your diabetes management efforts?" A cut-off of ≥ 40 in the PAID was used to determine whether more severe diabetes-specific emotional problems were

present (Pouwer *et al.*, 2005; Snoek *et al.*, 2000). A copy of the PAID is presented in Appendix 13.

Psychometric Properties of the PAID

Psychometric reports to date on the PAID have shown it to have consistently high internal reliability (Cronbach's alpha = .95) and to have sound two month test–retest reliability ($r = .83$) using a sample of patients. It was also demonstrated to correlate strongly with a wide range of theoretically related constructs such as general emotional distress, depression, diabetes self-care behaviours, diabetes coping, and health beliefs; and to be a statistically significant predictor of glycaemic control in a study that tracked HbA_{1c} for a diabetes population for one year (Snoek *et al.*, 2000; Welch *et al.*, 1995; Welch *et al.*, 2003; van der Ven *et al.*, 2003). Evidence of construct validity has been reported based on correlations with related measures, including diabetes coping scales (Welch *et al.*, 1995).

5.6 Ethical Considerations

5.6.1 Potential Distress to Participants

There are no known risks in completing self-report questionnaires about emotional distress, and they are administered routinely in a wide variety of studies including areas of palliative medicine and suicidal risk (Zimmerman *et al.*, 1995). Furthermore, both the HADS and the IES-R are also recommended by clinical guidance agencies such as National Institute of Clinical Excellence (NICE, 2005) and are used throughout the National Health Service as part of routine screening and service evaluation. However, all participants were reminded that they were free to withdraw at any time and that the author was available to discuss any concerns.

A system of care was put in place if a participant scored at clinically significant levels of psychological distress at follow-up (Appendix 14). The participants were advised at all stages of the project that they could speak with the author or other suitable health professional (such as their general practitioner), if they felt this would be helpful or if they were feeling overwhelmed.

5.6.2 *Informed consent*

As previously described, the participants were deemed to have capacity to consent as per the clinical judgement of senior members of the inpatient diabetes team prior to the author approaching the patient. When meeting participants for the first time, it was highlighted that they were free to withdraw at any time and that this decision would in no way affect their current or future care within the health service. The aims and process of the study were then outlined and the participant was asked whether they still wished to participate. If they agreed, they were provided with a consent form (Appendix 7) to read and 24 hours later should they wish to participate were asked to and sign.

5.6.3 *Confidentiality*

The confidential nature of all information collected throughout the study was emphasised to participants on the participant information sheet (Appendix 6) and during discussion on the ward. A series of measures was employed to ensure the highest standards of confidentiality. For the purpose of identification, each participant was assigned a unique number. All demographic data was then anonymised. This anonymised data was transferred onto a password-protected NHS computer. Returned questionnaires were stored safely in a locked filing cabinet. Each participant's unique identification number was the only link to their personal information. Personally identifiable data (e.g. name, date of birth, address) was stored in a locked filing cabinet on NHS premises. Only the researcher and her supervisors had access to this data. The author analysed the data using statistical software package developed for the social sciences (SPSS, Version 19). Data analysis took place in the author's office, using an NHS computer, on NHS premises. This SPSS database was kept on a password-protected computer at all times.

5.6.4 *Ethical approval*

An application for ethical approval was submitted to NHS Grampian North of Scotland Research Ethics Committee on 6 June 2011. Written confirmation of full ethical approval was received on 3 August 2011 (Appendix 5). Following this, the study was registered with NHS Grampian's Research and Development office, who

on 30 August 2011 gave their approval for the study to commence (Appendix 15). Indemnity cover was provided by the University of Edinburgh prior to the research commencing and by the NHS indemnity scheme.

5.6.5 Sample size

Sample size estimation depends on the anticipated strength of the relationships that are being explored (effect size) and the amount of statistical power required to be able to detect such effects (Field, 2005).

An estimated effect size for this study was calculated based on an effect size obtained by a well-designed study looking at PTSD symptoms at 3 month follow-up with a trauma-exposed group (Conlon *et al.*, 1998). The Cohen's *d* effect size obtained from this study was .87 (a large effect size). Although effect sizes in behavioural research are generally of medium size (Cohen, 1988), in the general trauma literature an acute stress reaction is commonly seen after a traumatic event and this typically attenuates over time (National Institute of Clinical Excellence (NICE), 2005). Therefore, it was deemed appropriate to base the calculation detecting a large effect size ($d = .87$) with statistical Power of .08 using parametric statistics 10 participants were required and non-parametric statistics, approximately 17 participants were required (Faul *et al.*, 2009).

5.7 Analytic plan

5.7.1 Hypotheses

It was hypothesised that

- (1) there would be a significant reduction in the number of participants reporting significant levels of emotional distress (PTSD; depression; anxiety; and diabetes related distress) between baseline and follow-up;
- (2) there would be a significant reduction in the median scores of emotional distress (PTSD; depression; anxiety and diabetes related distress) over time;
- (3) those admitted for DKA would have significantly higher levels of anxiety and/or depression (both median scores and level meeting caseness) than the overall local type 1 diabetes clinical population, and;

- (4) those admitted for DKA would have significantly higher levels of pre-existing HbA_{1c} than the overall local type 1 diabetes clinical population.

Checks of representativeness of sample

- (i) those who participated at baseline would not differ in terms of demographic or clinical variables compared with those who did not participate in the study
- (ii) those who completed the study would not differ in terms of demographic or clinical variables when compared with those who dropped out after baseline

5.7.2 Data screening

Exploratory data analysis was carried out to determine whether the assumptions for appropriate use of parametric statistics were met (Gravetter & Wallnau, 1996). To check whether the data was normally distributed, a frequency distribution was used to plot the data and check for the presence of outliers. Together with visual inspection of distributions, significant values ($p < 0.05$) in the Kolmogorov-Smirnov test were taken to indicate that the distribution was significantly different to the norm. As the data did not appear to meet assumptions for parametric statistics, non-parametric statistics were employed.

Non-parametric tests make fewer assumptions about the nature of the data population and can be appropriate for small data sets where assumptions of normality may not be met and where tests of normality lack power.

5.7.3 Analysis

Main statistics

The Wilcoxon matched pairs test was used to evaluate potential differences between pre-existing and baseline; pre-existing and follow-up, and baseline and follow-up HADS scores and between baseline and follow-up scores on the IES-R and PAID. McNemar's test was used to analyse potential differences over time in the proportion of participants falling in to case/ non-case categories for anxiety, depression and PTSD symptoms.

The Wilcoxon matched pairs test was also used to assess any significant difference between the pre-existing and follow-up HbA_{1c} values among those who completed the study. Only those who completed questionnaires at both time points were included in the analysis.

Comparison of study and non-study DKA admissions

Chi-square test was used to evaluate potential differences between males and females and in levels of deprivation. Fisher's exact test was used to explore any possible significant differences between pre-existing caseness for anxiety and depression. The Mann-Whitney *U* test was used to evaluate a range of potential differences between those admitted with DKA during the study period. This included exploring possible significant differences in: age; anxiety score; depression score; pre-admission HbA_{1c}; number of diabetes clinic appointments attended in the year preceding admission; length of stay in hospital, and duration since diabetes diagnosis.

Comparison of those who completed the study and those who dropped-out

The above tests were run for those who completed and those who dropped out. Mann-Whitney *U* test also was used to analyse the PAID and IES-R scores between those who completed and those who dropped out. In addition, Fisher's exact test was also used to explore any possible significant differences in caseness for PTSD between these two groups.

Comparison with local Type 1 diabetes clinical population

Chi-square test was used to evaluate differences in levels of deprivation for the DKA sample with the overall local type 1 clinic population.

The Fisher's exact test was used to explore potential differences between the study sample and the local type 1 diabetes clinical population in the prevalence of clinical levels of anxiety and depression. Mann-Whitney *U* Test was used to evaluate any differences in the continuous sample from the local type 1 diabetes clinical population and study sample scores for anxiety and depression.

The Mann-Whitney U Test was used to identify any differences in HbA_{1c} between the study sample and overall local type 1 diabetes clinical population.

6. JOURNAL ARTICLE

Title: Emotional sequelae during and following hospital admission for diabetic ketoacidosis in type 1 diabetes: a prospective, cohort study

Short Title: Emotional sequelae post diabetic ketoacidosis

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Word Count: 4,080

Keywords: anxiety, depression, post traumatic stress disorder, emotional outcomes, diabetes, complication

⁴ Dr Andrew Keen and Dr David Gillanders have author credit for the journal as supervisors and intellectual contributors but that the writing of the thesis is entirely the thesis author's

⁵ Dr Ann Gold authorised recruitment from the diabetes inpatient ward for the study

ABSTRACT

OBJECTIVE – The primary objective was to longitudinally investigate the levels of emotional distress among adults with type 1 diabetes during and post-discharge from hospital following successful treatment of diabetic ketoacidosis (DKA).

RESEARCH DESIGN AND METHODS - Questionnaires measuring anxiety, depression, post-traumatic stress disorder (PTSD) symptoms and diabetes related distress were completed at baseline (time of hospital discharge) and at 3 month follow-up. Statistical analyses were conducted to examine levels of emotional distress over time and its relationship to diabetes control. Additional demographic and clinical data was also collated and analysed.

RESULTS - 31 participants were recruited at baseline and 24 (77.4%) completed questionnaires at 3 month follow-up. Many participants reported clinical levels of anxiety (37.5%); depression (25%), and PTSD symptoms (37.5%) at baseline. At follow-up, the prevalence of clinical levels of anxiety remained high (37.5%), although the rates of clinical depression (8.3%) and PTSD symptoms (8.3%) attenuated markedly. There was no significant change in diabetes-related distress scores across time ($P = 0.055$). Pre-existing diabetes control was considerably poorer in the study sample than the overall local type 1 clinical population (10.9% versus 8.9%; $P < 0.0001$) and this did not improve following discharge ($P = 0.487$).

CONCLUSIONS - DKA is associated with a complex and clinically significant psychological reaction. In part, this is resolved in the months subsequent to discharge from hospital; however, clinical levels of anxiety remain commonplace. It is probable that these psychological problems during and after admission go undetected and therefore are not used routinely to inform management and intervention approaches. Further investigation is warranted to identify the longer-term course of emotional distress following DKA to inform any associated care pathway and raise awareness of psychological vulnerability of this sub-group of people with type 1 diabetes.

6.1 INTRODUCTION

Type 1 diabetes is associated with an increased prevalence of emotional distress when compared with the general population. Although there is some debate about exact figures, the reported prevalence rate of clinical anxiety is between 14% and 49% (approximately two to six times the general population) and of clinical depression is between 10% and 20% (about two to four times that of the adult population without diabetes) (1,2). Meta analytical studies have indicated that clinical anxiety and depression are associated with poorer diabetes control (HbA_{1c}) (3, 4) and therefore potentially affect both shorter- and longer-term health outcomes. There is evidence that depression is associated with poorer lifestyle choices (e.g. higher rates of smoking; more sedentary life-style; and less healthy diet) as well as a greater risk of macro-vascular and micro-vascular complications (5,6,7,8). Importantly, there is some evidence that successful treatment of depression can lead to not only better emotional wellbeing but also lower blood glucose levels (9, 10).

Diabetic ketoacidosis (DKA) is the most dangerous acute complication of type 1 diabetes (11), characterised by a triad of symptoms (hyperglycaemia, ketosis and acidosis), which can lead to coma and death. A common precipitant to DKA is poor control and compliance (12) highlighting substantial and enduring difficulties around self management. The underlying reasons for peoples' difficulties in effectively managing their condition vary. It is clear that many of the significant barriers to improved diabetes control relate to beliefs that people with diabetes have about themselves, their condition and also relate to emotional wellbeing. Typically, these factors are enmeshed.

It is commonplace that those admitted with DKA receive treatment in an Intensive Care Unit (ICU) (13). There has been an increasing interest in psychological outcomes of ICU survivors, and systematic reviews indicate a high prevalence of clinical levels of anxiety, depression and post-traumatic stress disorder (PTSD) symptoms in the months and years following hospital discharge (14, 15, 16). What remains unclear is whether ICU admission is an independent risk factor for emotional distress or if the elevated prevalence of post-ICU distress is confounded

by other factors such as sex, age or the lasting effects of medical conditions themselves, treatments and physical recovery processes.

Overall, there is reasonable evidence that there is considerable interplay between diabetes control and emotional wellbeing, and strong evidence of increased psychological problems among some of those discharged from ICU with non-diabetes related conditions. As far as the authors' are aware, there is no existing literature on the psychological outcomes among adults with diabetes following admission to ICU for DKA. The primary aim of this study therefore is to investigate the symptoms of anxiety; depression, PTSD and diabetes related distress among adults with type 1 diabetes discharged post DKA.

6.2 RESEARCH DESIGN AND METHODS

6.2.1 Design and methods

This is a prospective cohort study. The participants were enrolled from September 2011 to March 2012 within an ICU unit in an adult tertiary care university-affiliated hospital in the United Kingdom (Aberdeen Royal Infirmary, Scotland) and follow-up ended in July 2012. All patients presenting at admission with DKA (Ketonaemia 3 mmol/l and over or significant ketonuria, and blood glucose over 11 mmol/l or known diabetes mellitus and HCO₃ below 15 mmol/l and/or venous pH less than 7.3) as defined by National Health Service (NHS) Diabetes (17) were considered. Those with a pre-existing diagnosis of type 1 diabetes; fluent in English; the capacity to consent; with their acidosis corrected, and who were eating and drinking were eligible for inclusion in the study. All potential participants were approached prior to hospital discharge and informed, written consent was sought.

Demographic data (sex, age) and clinical data (duration of diabetes, previous DKA; number of contacts with the Diabetes team in year preceding DKA; precipitant to DKA; length of hospital stay; pre-existing levels of anxiety and depression) were obtained from medical records and SCI-DC Network (a national diabetes database).

The Scottish Index of Multiple Deprivation (SIMD) quintiles were used to describe the relative deprivation of those admitted for DKA, with group 1 being the most deprived and group 5 being the least deprived.

Participants completed the Hospital Anxiety and Depression Scale (HADS; 18), Impact of Events Scale-Revised (IES-R; 19) and Problem Areas In Diabetes (PAID; 20) at baseline (prior to hospital discharge) and follow-up (3 months later) (questionnaires were posted to participants). The HADS is a self-report screening questionnaire for anxiety and depression and a score of ≥ 11 on either the anxiety or depression sub-scale indicates clinically significant levels (or “caseness”). The IES-R is a 22-item self-report scale and a score of ≥ 33 is commonly assumed to indicate clinically significant levels of PTSD symptoms (21). The 20-item PAID was used to measure diabetes-related distress and higher scores represent greater distress (maximum score 100) and a cut-off of ≥ 40 to indicate severe levels of diabetes distress.

If there was one uncompleted item on each subscale of IES-R; HADS, or PAID then the missing item was allocated the mean of that sub-scale’s items, for that participant. This method was used for 1 participant questionnaire at baseline and 9 participant questionnaires at follow-up.

The HbA_{1c} value before admission (mean = 120 days; *SD* = 78.5) was collected to assess diabetes control prior to DKA. Similarly, to ascertain post-DKA control, the first HbA_{1c} value measured at least three months following discharge was obtained (mean=107 days; *SD* = 22.0).

6.2.2 Comparative data

The HbA_{1c} for all adults (excluding study participants) with type 1 diabetes in the Grampian region (N=2968) was obtained (referred to as the overall local type 1 diabetes clinical population herein) from SCI-DC Network and used to compare with the DKA sample.

Adults with type 1 diabetes who attend the Diabetes Centre in Aberdeen are screened annually for anxiety and depression using the HADS. A continuous sample

(excluding study participants) of HADS inventories collected over a three month period (n=390; 13% of overall type 1 diabetes clinic; referred to as the local type 1 diabetes clinical population herein) was collected and compared with the DKA study sample.

6.2.3 Power

To detect a medium effect size with the statistical power of 0.8 at alpha level of 0.05 using non-parametric statistics, approximately 17 participants were required (22).

6.2.4 Ethics

The NHS North of Scotland Regional Ethics Committee approved the study.

6.2.5 Statistical methods

The reporting of this study conforms to the STROBE (23) statement. All analyses were performed using SPSS (24).

Main statistics

The Wilcoxon matched pairs test was used to evaluate potential differences between pre-existing and baseline; pre-existing and follow-up, and baseline and follow-up HADS scores and between baseline and follow-up scores on the IES-R and PAID. McNemar's test was used to analyse potential differences over time in the proportion of participants falling in to case/ non-case categories for anxiety, depression and PTSD symptoms. The Wilcoxon matched pairs test was also used to assess any significant difference between the pre-existing and follow-up HbA_{1c} values among those who completed the study. Only those who completed questionnaires at both time points were included in the analysis.

Comparison of study and non-study DKA admissions

Chi-square test was used to evaluate potential differences between males and females and in levels of deprivation. Fisher's exact test was used to explore any possible significant differences between pre-existing caseness for anxiety and depression. The Mann-Whitney *U* test was used to evaluate a range of potential differences between

those admitted with DKA during the study period. This included exploring possible significant differences in: age; anxiety score; depression score; pre-existing HbA_{1c}; number of diabetes clinic appointments attended in the year preceding admission; length of stay in hospital, and duration since diabetes diagnosis.

Comparison of those who completed the study and those who dropped-out

The above tests were run for those who completed and those who dropped out. Mann-Whitney *U* test also was used to analyse the PAID and IES-R scores between those who completed and those who dropped out. In addition, Fisher's exact test was also used to explore any possible significant differences in caseness for PTSD between these two groups.

Comparison with local type 1 diabetes clinical population

Chi-square test was used to evaluate differences in levels of deprivation for the DKA sample with the overall local type 1 clinic population. The Fisher's exact test was used to explore potential differences between the study sample and the local type 1 diabetes clinical population in the prevalence of clinical levels of anxiety and depression. Mann-Whitney *U* Test was used to evaluate any differences in the continuous sample from the local type 1 diabetes clinical population and study sample scores for anxiety and depression. The Mann-Whitney *U* Test was used to identify any differences in HbA_{1c} between the study sample and overall local type 1 diabetes clinical population.

6.3 RESULTS

6.3.1 Participant characteristics

Figure 6.1 describes the recruitment and eligibility requirement for the study sample. Participant characteristics are detailed in Table 6.1 No significant difference observed between the study sample and the overall type 1 diabetes clinical population for deprivation ($P^{\delta} = 0.841$).

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6.3.2 Comparison of study and non-study DKA admissions

Forty-seven patients were eligible to participate and 31 were recruited at baseline (see Figure 6.1). Although a greater percentage of those who chose to not participate were male (60%), the difference between male and female participation rates was not significant ($P = 0.174$). Similarly, there was no significant difference between the ages of those who chose to participate and those who did not (median = 26 (interquartile range (IQR) = 22.0) vs. 27 (IQR = 23.0) years; $P = 0.598$); their pre-existing HbA_{1c} (median = 11.4% (IQR = 4.0) vs. 12.1% (IQR = 5.1); $P = 0.639$); SIMD quintile distribution ($P = 1.000$); length of hospital stay (median = 2 (IQR = 2.0) vs. 3 days (IQR = 1.0); $P = 0.076$); pre-existing HADS anxiety score (median = 7.0 (IQR = 8.0) vs. 9.5 (IQR = 6.8); $P = 0.268$); pre-existing HADS anxiety caseness ($P = 0.295$); pre-existing HADS depression score (median = 3.0 (IQR = 7.0) vs. 8 (IQR = 3.8); $P = 0.184$); and, pre-existing HADS depression caseness ($P = 0.553$). Significant differences between those who participated in the study and those who did not were observed in the number of attended diabetes clinical appointments in the year preceding DKA (median = 2 (IQR = 2) vs. 0 (IQR = 1) days; $P = 0.002$) and in the duration of diabetes (median = 8 (IQR = 9) vs. 15 years (IQR = 6); $P = 0.005$).

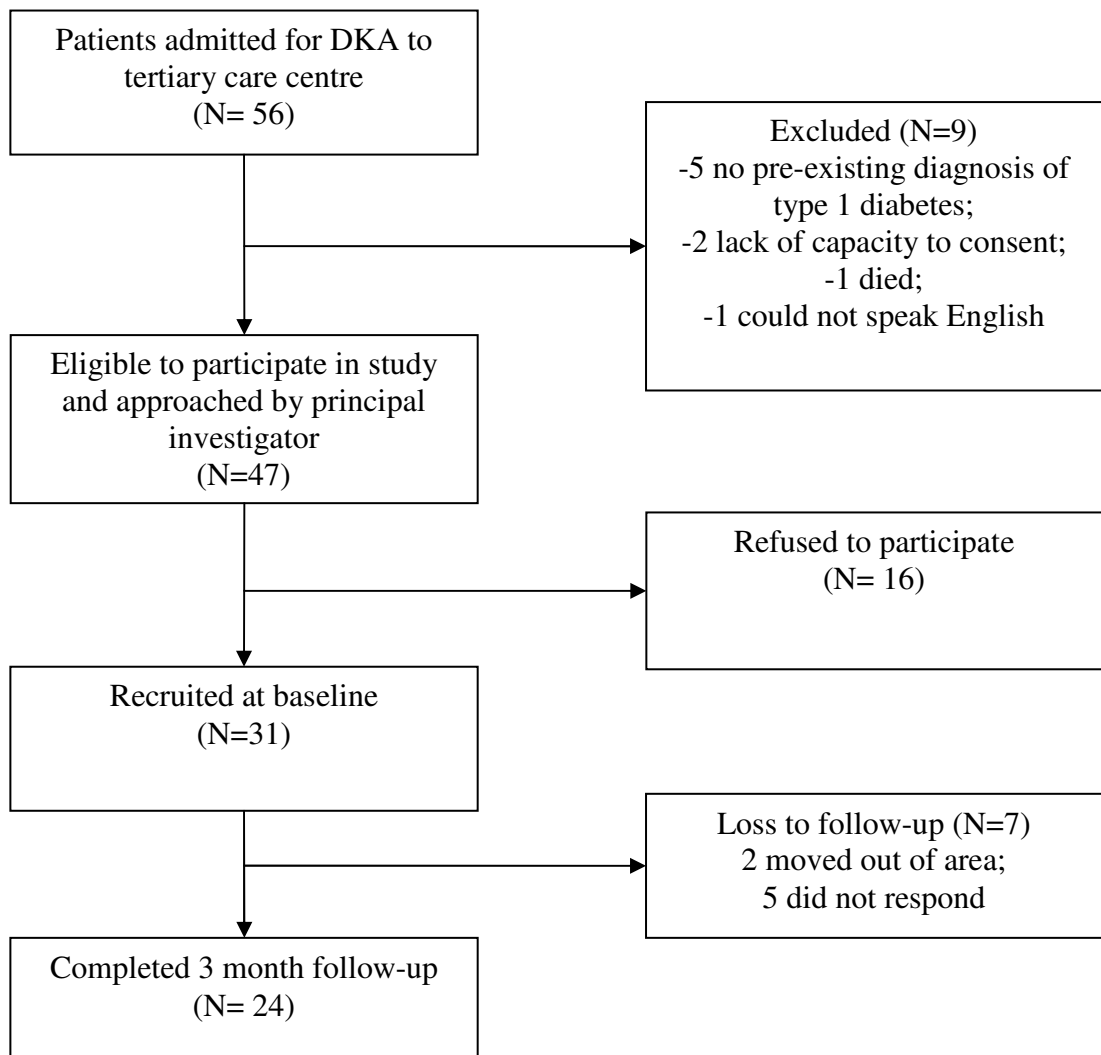


Figure 6.1 – *Flow diagram of recruitment and retention of participants*

Table 6.1 – Patient characteristics

Parameter	Baseline	Follow-up
Number of patients	31	24
Female gender, %, n	61.3%, 19	66.7%, 16
≤ 21 years of age, %, n	35.5%, 11	41.7%, 10
Diagnosis in preceding year, %, n	16.1% , 5	12.5%, 3
Previous admission for DKA, %, n	58.1% , 18	62.5%, 15
Precipitant to DKA as noted by Diabetes Team, %, n		
• Infection	35.5%, 11	45.9%, 11
• Alcohol misuse	29.0%, 9	16.7%, 4
• Gastrointestinal problems	22.6%, 7	29.2%, 7
• Missed insulin	9.7%, 3	8.3%, 2
• Myocardial infarction	3.2%, 1	-
SIMD Quintile, %		
• 1 (most deprived)	3.2%, 1	4.2%, 1
• 2	19.4%, 6	20.8%, 5
• 3	19.4%, 6	12.5%, 3
• 4	29.0%, 9	29.2%, 7
• 5 (least deprived)	29.0%, 9	33.3%, 8

6.3.3 Comparison of those recruited who completed the study and those who dropped out

A total of 31 eligible patients completed baseline questionnaires and of these 24 (77.4%) completed the questionnaires at 3 months. There were no significant differences between participants completing the study and those who dropped out with respect to sex (57.1% of those lost to follow up were males; $P = 0.255$); deprivation ($P = 1.000$); age (median = 25.5 (IQR = 26.3) vs. 28 (IQR = 20.0) years; $P = 0.636$); length of hospital stay (median = 3 (IQR = 2) vs. 3 (IQR = 1) days; $P = 0.142$); duration of diabetes (median = 9 (IQR = 9.8) vs. 4 (IQR = 10) years; $P = 0.102$); pre-existing HbA_{1c} (median = 10.9% (IQR = 5.5%) vs. 12.0% (IQR = 5.1%); $P = 0.069$); baseline HADS anxiety score (median = 7 (IQR = 7.5) vs. 12 (IQR = 8); $P = 0.245$); baseline anxiety caseness ($P = 0.413$); baseline HADS depression score (median = 5 (IQR = 9) vs. 10 (IQR = 6); $P = 0.052$); baseline depression caseness ($P = 0.384$); baseline IES-R score (median = 18.5 (IQR = 26.5) vs. 25.0 (IQR = 23.0); $P = 0.309$), or baseline PTSD caseness ($P = 1.000$). However, those who completed

the study had significantly lower levels of diabetes related distress than those who dropped out (median = 40.6 (IQR = 27.2) vs. 66.3 (IQR = 16.3); $P = 0.026$).

6.3.4 Emotional distress

Figure 6.2 shows the percentage of study participants at baseline and follow-up scoring at clinically significant levels for anxiety (37.5% vs. 37.5%), depression (25% vs. 8.3%) and PTSD (37.5% vs. 8.3%) symptoms.

The percentage of the local type 1 diabetes clinical population meeting clinical levels for anxiety and depression were 11.9% and 6.0%, respectively. Pre-existing levels of anxiety (16.7%) and depression (16.7%) were available for 19 of the study completers. The median time prior to admission that these scores collated was 314 days.

6.3.5 Anxiety

DKA sample

Overall, there was no significant difference between pre-existing and baseline anxiety scores ($P = 0.264$) and proportion meeting caseness ($P = 0.500$). No significant difference was found between the pre-existing and follow-up anxiety scores (median at follow-up = 8 (IQR = 9.5); $P = 0.735$) or between anxiety scores at baseline and follow-up ($P = 0.294$). Similarly, there was no significant difference between the proportion of participants experiencing clinical levels of anxiety at baseline and follow-up (for both groups 37.5%; $P = 1.000$). Eighty-nine percent of those who initially had clinical levels of anxiety continued to be clinically anxious three months later (which was about one in three of DKA admissions overall).

DKA sample compared with clinic

Those admitted for DKA had significantly higher levels of anxiety at baseline ($P = 0.001$) and follow-up than the local type 1 diabetes clinical population (clinical median = 5 (IQR = 5); $P = 0.015$). There was no significant difference in the anxiety scores of the local type 1 diabetes clinical population and pre-existing levels of anxiety ($P = 0.135$). A significantly higher proportion of study participants met

caseness at baseline and follow-up than the local type 1 diabetes clinical population (clinic proportion = 11.8%; $P = 0.0018$).

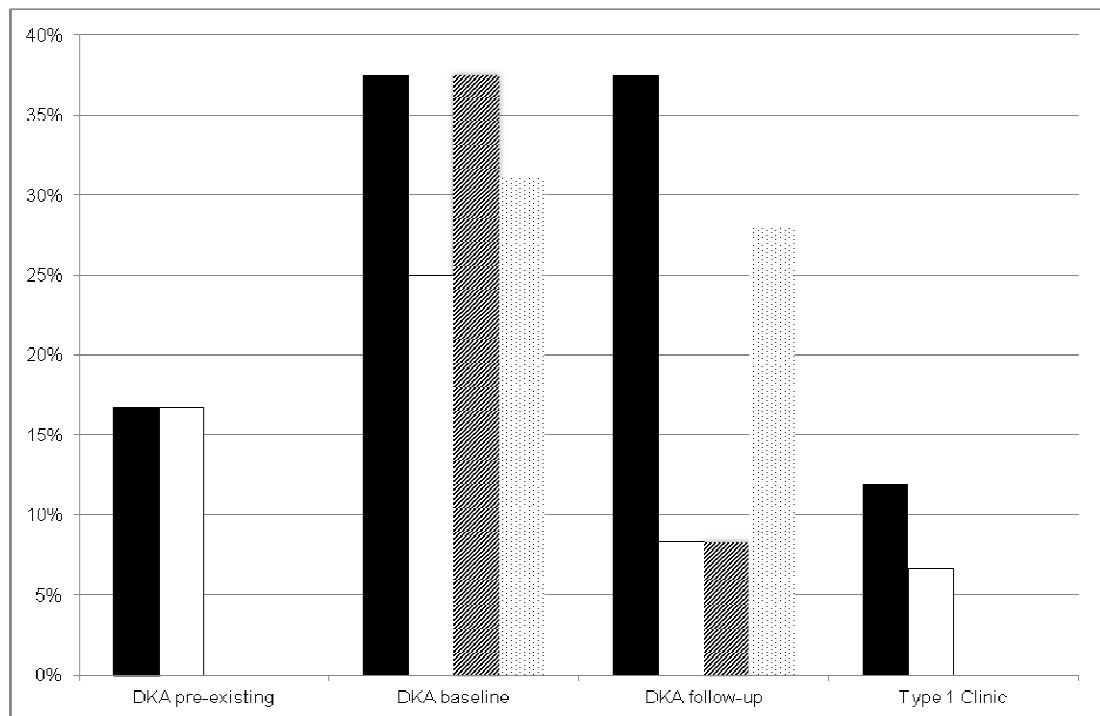


Figure 6.2 – The percentage of study participants meeting caseness for anxiety (■) and depression (□) pre-existing ($n=19$), baseline ($n=24$) and follow-up ($n=24$); the percentage meeting caseness for PTSD symptoms (▨) at baseline ($n=24$) and follow-up ($n=24$); the percentage meeting cut-off for severe diabetes distress (▩) and the percentage of local type 1 diabetes clinical population ($n=390$) meeting caseness for anxiety and depression.

6.3.6 Depression

DKA sample

No significant differences were observed between pre-existing and baseline depression scores (baseline median = 5 (IQR = 9.5); $P = 0.896$) or pre-existing and follow-up depression scores (median at follow-up = 5 (IQR = 7); $P = 0.250$). There was no significant difference in depression scores from baseline to 3 months ($P =$

0.205), nor was there any significant change in the proportion of participants experiencing clinical levels of depression (25% vs. 8.3%; $P = 0.125$). Of those initially reporting clinically significant levels of depression, 33.3% continued to do so 3 months later.

DKA sample compared with clinic

There was no difference between the DKA sample baseline depression scores and the local type 1 diabetes clinical population (median = 2; $P = 0.010$) or in the pre-existing depression scores (16.7%) and the depression scores of the local clinical type 1 diabetes clinical population ($P = 0.654$). However, compared to the local type 1 diabetes clinical population, a significantly higher proportion of participants crossed the threshold for caseness at baseline ($P = 0.0003$) but not at follow-up ($P = 0.6721$).

6.3.7 PTSD

There was a significant reduction in PTSD symptom scores between baseline and follow-up (median = 18.5 (IQR = 26.5) vs. 12 (IQR = 20.0); $P = 0.006$) and in the proportion of participants experiencing clinical levels of PTSD symptoms at baseline and follow-up (37% vs. 8%; $P = 0.016$). The majority (seven out of nine; 78%) of those initially exhibiting clinical levels of PTSD symptoms did not do so at follow-up.

6.3.8 Diabetes related distress

No significant difference was found between baseline and follow-up PAID scores (median = 40.63 (IQR = 27.19) vs. 38.75 (IQR = 21.88); $P = 0.055$). Thirty-one percent met severe levels for diabetes related distress at baseline and 28% at follow-up.

6.3.9 Co-morbidity

Figure 6.3 illustrates the percentage of participants who scored at clinically significant levels for anxiety; depression, and PTSD symptoms as well as all possible

combinations of the three conditions. In all instances, where there were clinical levels of depression or PTSD, clinical anxiety was similarly present.

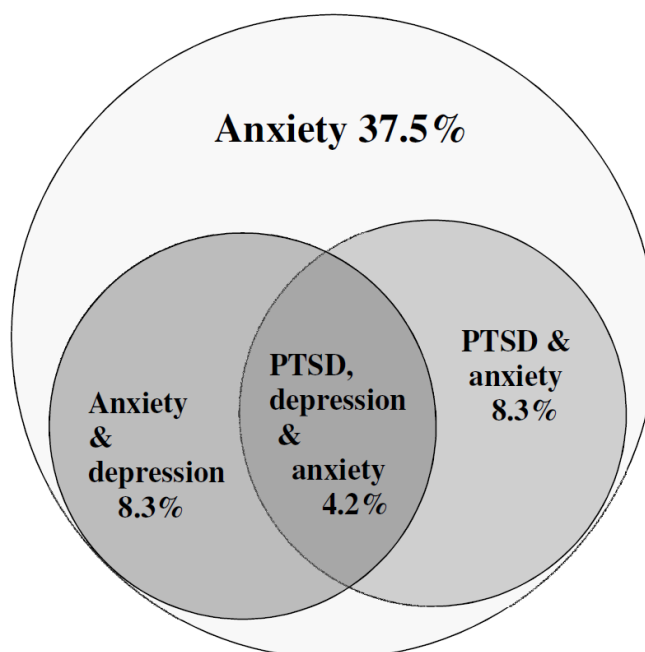


Figure 6.3 – *Co-morbidity of clinical levels emotional distress at 3 month follow up*

6.3.10 Diabetes control

DKA sample

There was no significant change in diabetes control from pre-existing to follow-up ($n = 15$; follow-up median 10.6% (IQR = 6.1%); $P = 0.487$).

DKA sample compared with clinic

The study sample had significantly higher pre-existing HbA_{1c} values than the overall local type 1 diabetes clinical population (median = 10.9% (IQR = 5.5%) vs. 8.9% (IQR = 2.1%); $P < 0.0001$).

6.4 CONCLUSIONS

6.4.1 Main outcomes

This is, to the authors' knowledge, the first follow up study of emotional distress following hospital admission for DKA, and the results indicate that there was substantial psychological morbidity. Almost four in ten participants reported clinical levels of anxiety three months after discharge, which is three times higher than the overall type 1 diabetes clinical population. Although the rate of caseness for depression was initially substantial (one in four) this fell markedly consistent with the local adult type 1 diabetes clinical population (about one in twelve). A similar pattern occurred among those who initially reported clinical levels of PTSD symptoms, with approximately seven in nine no longer reporting caseness at follow-up. Overall, the results indicate that DKA admission is associated with an acute post-traumatic stress and depressive reaction which dissipates, and an anxiety reaction that appears to be longer-lasting.

6.4.2 Anxiety

It is striking that anxiety rather than depression appears to be the dominant feature of those admitted for DKA. Although there is some evidence that anxiety does influence HbA_{1c} values (4) there has been more interest on the role of depression in diabetes self-management (e.g. 3,5). There are sound theoretical reasons why anxiety is associated with poorer control. For instance, when the body deals with stress the neuroendocrine system is activated and of particular importance is the hypo-pituitary-adrenal axis (HPA) (25). Both diabetes and anxiety may be associated with an increased, prolonged and hyper-activation of the HPA (resulting in release of glucose in to the bloodstream), which makes it more difficult to control blood glucose levels (25). To complicate matters further, there is considerable overlap between symptoms of anxiety and symptoms of hypoglycaemia (e.g. increased irritability and physiological symptoms such as hot flushes and shaking) (26). Thus symptoms of anxiety can be misinterpreted as indicating low blood glucose and thereby lead to inappropriate self-care interventions, which in turn can raise blood glucose levels unnecessarily. It may be the case that admission for DKA results in an increased

focus of attention on potential complications and their implications, exacerbating (and maintaining) high levels of anxiety. These types of worries (characteristic of anxiety) are compounded by the fact that routine HbA_{1c} values are relatively high. That is, in part at least these fears are realistic and evidence-based (whereas most worries associated with anxiety disorders are imaginary and unlikely to occur).

6.4.3 Depression

Clinical levels of depression at three month follow up are consistent with the local type 1 diabetes clinical population (6.7%) and prevalence is frequently cited between 10- 20% in the literature (2). Although not statistically significant, there is a substantial reduction in the number of participants reporting caseness for depression at follow-up (from 25% to 8.3%). This is all the more salient because the follow-up figure is lower than the pre-existing rate (16.7%). It is unclear what accounts for this reduction in clinical depression, although it could be the case that an acute lowering of mood is a natural response to what is often a very frightening, uncomfortable and unpleasant experience.

6.4.4 Diabetes Control

Perhaps unsurprisingly, those admitted for DKA had poorer diabetes control than the local type 1 population, indicating on-going difficulties with self-management. These findings are consistent with previous studies of DKA samples (e.g. 27).

6.4.5 Findings in wider context

Our study found clinical levels of anxiety in 37.5% of participants at follow-up, while 8.3% met cut-off for PTSD and depression. Studies tracking emotional distress three months following ICU discharge report lower levels of clinical anxiety (24% to 28%); higher levels of clinical depression (20% to 24%) and considerably higher levels of clinically significant PTSD symptoms (45% to 52%) (28, 29). Notably, these studies used lower thresholds to indicate clinical levels of anxiety; depression, and PTSD symptoms (e.g. HADS anxiety ≥ 8) than the current study which used conservative thresholds (HADS anxiety or depression ≥ 11 , and IES-R ≥ 33). The emotional distress profile at three months follow-up is relatively consistent with that

reported following the diagnosis of a chronic health condition. For example, among a group of adults diagnosed with prostate cancer, consistently high levels of anxiety were observed over time (30) and among a sample newly diagnosed with multiple sclerosis, depression levels were initially high however ameliorated over subsequent months (31).

6.4.6 Limitations

There are a number of limitations to this study. We have reported on a relatively small cohort from one centre. There was some evidence that the study sample was dissimilar to overall DKA admissions, for example, they attended routine diabetes clinic appointments more regularly. However, we found no significant difference on many variables investigated, and our recruitment and retention rates (66% and 77%, respectively) compare favourably to other studies of this type (28).

The dataset for pre-existing levels of emotional distress was incomplete (which indicates they either did not attend appointments over the preceding year or declined to complete the questionnaire, the latter of which is very uncommon). This group without recorded HADS may represent an unusually vulnerable group who has disengaged with local diabetes services. Moreover, follow-up diabetes control data was also incomplete probably for similar reasons.

6.4.7 Clinical implications and future research

Our results demonstrate that this group is particularly vulnerable. A greater awareness of the psychological issues affecting people with type 1 diabetes who experience DKA is required. Moreover, a better understanding of the ways in which emotional distress can impact on one's self management is needed as well as further investigation on how best to communicate this information in light of possible information processing deficits which may be a result of emotional distress.

Larger, multi-site, longer term follow-up studies, perhaps across multiple countries with different health care systems, are required to gain a greater understanding of the emotional difficulties endured by survivors of DKA. In particular, there is a dearth of

research on the role of anxiety in efforts of people with type 1 diabetes to manage their condition.

Although our data suggests that depression and PTSD symptoms largely self-resolve, further studies, similar to this study, should be carried out to gain a greater insight into the trend of emotional distress post DKA. To date it is unclear whether or not the trend over time of emotional distress is similar to that among the general population, or perhaps has a more chronic course.

Historically, the clinical management of DKA has focused on medical issues. However, there is clearly a considerable psychological component that can influence decisions about current and future care following successful treatment of DKA. For example, people experiencing PTSD symptoms typically do their best to avoid re-experiencing the traumatic event which includes being disinclined to talk or think about it (this could be why we found lower than expected levels of depression). Moreover, people exhibiting symptoms of depression are commonly lacking in energy and motivation, have a tendency to ruminate and feel hopeless. It is therefore easy to understand why it may be problematic to engage this sub-group. Difficulties include gathering information about their self-care regimens and decision-making; providing information that is relevant and facilitating helpful changes in health-related behaviour.

A systematic approach to identifying and helping those admitted for DKA who have clinically significant psychological problems that are enduring (this study indicates that anxiety might be the main emotional problem) would likely be beneficial to people with diabetes; their families, and health care providers. Especially in light of the marked rise of adult DKA admissions to NHS Scotland from 2003 (one year; n = 927) to 2009/10 (one year; n > 2000) (32, 33). These findings are not isolated to Scotland as they are consistent with epidemiological studies in the USA. (34). Moreover, there may be scope for multi-disciplinary interventions targeting this group who appear vulnerable to emotional distress; chronic poor control, and therefore substantial health problems in the future including premature death.

6.4.8 Summary

Overall, the results of this study suggest an acute PTSD-like and depressive reaction following DKA is common but subsides, whereas clinical levels of anxiety seems to persist over time. Further investigation of the course of emotional distress post DKA is warranted, including looking at psychological outcomes in a larger sample and over a longer period. This preliminary research suggests that those admitted for DKA require psychological as well as medical support. Innovative, multi-professional care provided in a systematic manner may well be necessary for this especially vulnerable group.

6.5 Acknowledgements

K.Y.M. researched the data, wrote the manuscript and researched data. A.J.A. and D.G. reviewed/edited the manuscript.

There are no conflicts of interest to declare.

As the corresponding author K.Y.M takes full responsibility for the work as a whole.

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Appendix 1

Guidelines for submission to *Journal of Critical Care*

http://www.elsevier.com/wps/find/journaldescription.cws_home/623143/authorinstructions

Journal of Critical Care

Improving Patient Care by Integrating Critical Care Systems Knowledge into Practice Behavior

Guide for Authors

The *Journal of Critical Care* provides a forum for the publication of original peer-reviewed articles with the goal of improving patient care by integrating critical care systems knowledge into practice behavior. The journal represents the World Federation of Societies of Intensive and Critical Care Medicine (WFSICCM), an organization of 42 national intensive/critical care societies representing some 32,000 physicians and allied health professionals. With this responsibility to the WFSICCM comes an international focus in systems research in constrained resource environments.

We accept research articles and review articles as well as those in a seminar or tutorial format. Topics covered are all aspects of Health Services Research, the interface of critical care, anesthesiology, and pain, as well as tutorials for residency education core competencies.

For the seminar format, the articles should be directed to the resident or practicing healthcare professional. We are particularly interested in your up-to-date evaluation of the topic. Dealing with subjects of current and sometimes controversial educational and research themes is acceptable. The seminar format lends itself to a more informal presentation. Express your own viewpoints, but feel free to discuss other viewpoints as well. If you are uncertain, please indicate the degree of your uncertainty. We are looking for an absolutely honest evaluation of the topic.

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Authors who are unable to provide an electronic version or have other circumstances that prevent online submission must contact the Editorial Office prior to submission to discuss alternate options. The Publisher and Editors regret that they are not able to consider submissions that do not follow these procedures.

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Preparing the manuscript

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- Arial 10 or New Roman 12 font,
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The first page of the manuscript must contain the following information:

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- 2) author names;
- 3) name of the institution in which work was done;
- 4) acknowledgments for research support;
- 5) name and address of the author to whom communications should be directed.

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- 3-5 keywords
- 100-200 word abstract

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Journal article:

Eissa NT, Ranieri VM, Corbeil C, et al: Effects of positive end-expiratory pressure on the work of breathing in adult respiratory distress syndrome patients. *J Crit Care* 1992; 7:142-149

Journal article in press

Marini JJ, Ravenscraft SA: Mean airway pressure--Physiologic determinants and clinical importance: Parts 1 and 2. *Crit Care Med* (in press)

Abstracts

Wang P, Ba ZF, Chaudry IH: ATP-MgCl₂ improves renal function following severe hemorrhagic shock. *FASEB J* 28:A1085, 1990 (abstr)

Editorials

Tracey KJ, Lowry SF, Cerami A: Cachectin/TNF-alpha in septic shock and septic adult respiratory distress syndrome. *Am Rev Respir Dis* 138:1377-1379, 1988 (editorial)

Complete book

Scharf SM: *Cardiopulmonary Physiology for Critical Care*. New York, NY, Marcel Dekker, 1992

Chapter of book

Reynolds HY: Normal and defective respiratory host defenses, in Pennington JE (ed): *Respiratory Infections: Diagnosis and Management* (ed 2). New York, NY, Raven, 1989, pp 1-33

Chapter of book that is part of a published meeting

Till GO, Warren SS, Gannon DE, et al: Effects of pentoxifylline on phagocytic responses in vitro and acute and chronic inflammatory reactions in vivo, in Mardell G, Novick W (eds): *Pentoxifylline and Leukocyte Function, Proceedings of a Symposium*. Sommerville, NJ, Hoechst-Roussel Pharmaceuticals, 1988, pp 124-127

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Announcements of meetings, conferences, and the like that are of interest to the readership of the *Journal of Critical Care* should be sent to the Editor at least three months before the first day of the month of issue.

Revised February 2012

Appendix 2

Guidelines for submission to *Diabetes Care*

***Diabetes Care* Instructions for Authors**

Last updated on February 29, 2012.

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- 3) Pathophysiology/Complications
- 4) Cardiovascular and Metabolic Risk

The journal also publishes clinically relevant Review Articles, Letters to the Editor, Brief Reports, and health/medical news or points of view. Topics covered are of interest to clinically oriented physicians, researchers, epidemiologists, psychologists, diabetes educators, and other health professionals. The journal does not publish descriptions of study designs without data, papers on in vitro studies, or studies involving animals.

The editor-in-chief of *Diabetes Care*, William Cefalu, MD, began his term with the January 2012 issue. Dr. Cefalu's editorial team began reviewing first submissions on July 1, 2011.

Editorial Note: Due to an increasing number of submissions and limited editorial space, manuscripts will initially be reviewed by an editorial committee and/or the editor. Manuscripts that exceed the word limit will be automatically declined, and only those that meet a priority score above the 50th percentile will be reviewed.

2. POLICIES

ADA's Publications Policy Committee follows the recommendations of the International Committee of Medical Journal Editors (ICMJE), the World Association of Medical Editors (WAME), and the Committee on Publication Ethics (COPE) for guidance on policies and procedures related to publication ethics. The policies for *Diabetes Care* have been adopted from those three advisory bodies and, where necessary, modified and tailored to meet the specific content, audiences, and aims of *Diabetes Care*. Comprehensive information related to the editorial and ethical policies of *Diabetes Care* can be found in [Publication Policies and Procedures for Diabetes Care](#). The Association's Publications Policy Committee or Subcommittee on Ethical Scientific Publications will consider on a case-by-case basis policies that are not addressed in the policies document, which contains information related to the following topics:

Study Design

Originality and Prior Publication

Authorship and Contributions

Acknowledgments

Conflict of Interest

Data Access and Responsibility

Clinical Trials, Systematic Reviews, and Meta-Analyses

Plagiarism

Digital Image Manipulation

Responses to Possible Scientific Misconduct

Peer Review

Editorial Decisions

Prepublication of Accepted Articles

Reuse, Post-Prints, and Public Access

Errata

Media Embargos

Advertising

Supplements

Frequently referenced segments of the document appear below.

2.1. All human investigation must be conducted according to the principles expressed in the Declaration of Helsinki. All studies involving animals must state that guidelines for the use and care of laboratory animals of the authors' institution or the National Research Council or any national law were followed.

Diabetes Care publishes only material that has not been published previously (either in print or electronically) and is not under consideration for publication elsewhere, with the exception of an abstract that is less than 400 words in length. Prior presentation of data (e.g., at a scientific meeting or via webcast) does not preclude publication in *Diabetes Care*, but should be disclosed in the Acknowledgments of the paper and in the author's comments to the editor upon manuscript submission. All submissions to the journal will be scanned for possible duplicate or prior publication using the CrossCheck/iThenticate plagiarism detection system (www.ithenticate.com/). Any article that eclipses a certain similarity threshold with another article will be closely reviewed by ADA. Authors who submit previously published work to the journal will be banned from submitting future manuscripts to the journal, and their funding body and/or institution will be notified.

All contributions, including solicited articles and symposia, are critically reviewed by the editors and/or invited referees. Reviewers' comments are usually provided to the authors. The decision of the editors is final.

2.2. Prepublication of accepted articles. To make new research readily available to subscribers, *Diabetes Care* publishes accepted articles online ahead of print weeks

before the print/online issue becomes available. These articles have been copyedited, proofread, and typeset but not yet author-approved or finalized and will appear in a future issue of *Diabetes Care* in print and online.

Online Ahead of Print articles are citable by unique DOI (digital object identifier). DOIs for *Diabetes Care* articles begin with 10.2337, followed by the article number assigned when the manuscript was submitted online via the manuscript submission system. (e.g., 10.2337/dc11-1234)

Example: Kohler C, Norton H, Farber K, Briggs E: How to cite a republished article in ADA journals. *Diabetes Care* 10.2337/dc11-1234

2.3. Embargo dates. If you are interested in reporting on a *Diabetes Care* online-ahead-of-print article, please visit

<http://care.diabetesjournals.org/misc/embargoinfo.pdf> for specific instructions and conditions. Articles that were not republished are embargoed until they appear in an issue of *Diabetes Care* Online.

2.4. NIH's PubMed Central. Beginning with the July 2008 issue, the American Diabetes Association will deposit all final print articles accepted for publication in *Diabetes Care* in PubMed Central, a repository of peer-reviewed research maintained by the National Institutes of Health. ADA provides this service at no cost to authors. Articles are accessible on PubMed Central 12 months after the date of final publication in *Diabetes Care*. Authors may submit the accepted version of their *manuscript* to their funding body's repository immediately upon acceptance.

2.5 Clinical Trials. The International Committee of Medical Journal Editors (ICMJE) defines a clinical trial as "any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes." All clinical trials submitted to *Diabetes Care* must be registered with an approved ICMJE clinical trial registry (ClinicalTrials.gov, www.ISRCTN.org, www.actr.org.au, www.umin.ac.jp, and www.trialregister.nl), *Diabetes Care* accepts registration of clinical trials in any of the primary registers that participate in the [WHO International Clinical Trial Registry Platform](http://www.who.int/trialregistry). Posting clinical trial results exceeding more than 500 words in the clinical trials registry is considered prior publication. Posting results in the form of a structured abstract (less than 500 words) or table is not considered prior publication. For definitions and further information, please see ICMJE's clinical trials registration policy found in ICMJE's [Uniform Requirements for Manuscripts Submitted to Biomedical Journals](http://www.icmje.org/Uniform_Requirements_for_Manuscripts_Submitted_to_Biomedical_Journals). Please be sure to include the unique trial number and the name of the registry (e.g., NCTXXXXXXXX, ClinicalTrials.gov; or ISRCTNXXXXXXXX, www.ISRCTN.org) on the manuscript's title page.

3. EDITORIAL OFFICE CONTACT INFORMATION

Diabetes Care Editorial Office

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e-mail: diabetescare@diabetes.org

Lyn Reynolds, Director, Editorial Office

Shannon Potts and Jane Lucas, Peer Review Managers

Rita Summers, Editorial Assistant

Joan Garrett, Editorial Secretary

4. FORMS AND REQUIREMENTS

4.1. Each corresponding author, including those of letters, must read all three sections, check the appropriate boxes, sign, and be sure to include the names of all authors on the [Manuscript Submission Form](#). The manuscript submission form addresses ADA's policies on 1) originality and authorship, 2) copyright assignment, and 3) potential conflict of interest and addresses permission policies related to **reuse** and **post prints**. ADA will accept ICMJE's [Uniform Disclosure Form for Potential Conflicts of Interest](#).

It is recommended that manuscript submission forms be scanned and uploaded with the article files. If this is not possible, the corresponding author may fax (317-859-3592) or email the completed form for all authors to the Editorial Office immediately after submission. Submissions will not be considered complete until the form has been received.

The **corresponding author** designated on the title page will be the only person notified when proofs become available. (For further information, see [Submitting a Manuscript](#) Section 7.1.1)

4.2. **Statement of Originality and Authorship.** *Diabetes Care* subscribes to the requirements stated in the [Uniform Requirements for Manuscripts Submitted to Biomedical Journals](#) that authorship implies substantial contributions to conception and design or analysis and interpretation of data and drafting of the article or critical revision for important intellectual content. The editor reserves the right to query authorship contribution.

Writing groups: All collaborators should be listed at the end of the paper in the Acknowledgments (if no more than two or three short paragraphs) or in a separate supplemental online-only file.

Author contribution paragraph: As of March 1, 2010, authors are required to include a paragraph in the Acknowledgments section listing each author's contribution.

Example: "C.K. researched data. L.R. wrote the manuscript and researched data. H.N. reviewed/edited the manuscript. V.S. contributed to the discussion and reviewed/edited the manuscript. N.B. researched data and contributed to discussion. V.G. wrote the manuscript."

Affiliations of those mentioned in the Acknowledgments section must also be noted.

When citing "editorial assistance" or help provided by a colleague, authors are required to list the employer/institution with which that colleague is affiliated.

Example: "The authors acknowledge the editorial assistance of Mark Smith, Global Informatics, Inc.;" "The authors thank Mark Smith, Global Informatics, Inc., for help with preparing the manuscript."

4.3. **Copyright Assignment.** The American Diabetes Association holds the copyright on all material appearing in *Diabetes Care*, unless the content is produced by an employee of the U.S. government as part of the authors' official duties. All authors must check the appropriate boxes and sign the Manuscript Submission Form, which transfers copyright to the ADA in accordance with the Copyright Revision Act of 1976. Please see the revised policy below for the **statement of provenance** and other conditions.

4.3.1. **Reuse.** Authors are permitted to reuse portions of their ADA-copyrighted work in their own work, including tables and figures, and to reuse portions or all of their

ADA-copyrighted work for lecture or classroom purposes, provided that the proper citation and copyright information is given.

4.3.2. Post-prints. Authors are permitted to submit the accepted version of their *manuscript* to their funding body or institution for inclusion in that funding body or institution's database, archive, or repository, or to post the accepted version on their personal Web site. These manuscripts may be made freely accessible to the public upon acceptance, provided that the following two conditions are observed: First, post-prints must include the following statement of provenance and, once the final version has been published in the journal, a link to the final published version of the paper on the journal's Web site:

This is an author-created, uncopyedited electronic version of an article accepted for publication in *Diabetes Care*. The American Diabetes Association (ADA), publisher of *Diabetes Care*, is not responsible for any errors or omissions in this version of the manuscript or any version derived from it by third parties. The definitive publisher-authenticated version will be available in a future issue of *Diabetes Care* in print and online at <http://care.diabetesjournals.org>.

Second, the version of the manuscript deposited or posted must be identical to the final accepted version, with the exception of the addition of the above statement and any changes necessary to correct errors. Authors may make changes to the posted version to correct mistakes or may issue an erratum at any time. However, the final published version of the manuscript may not be deposited, posted, or later substituted for the post-print.

4.4. Conflict of Interest statement. All authors must read the [ADA Policy Statement on Duality of Interest](#) and check the appropriate box on the [Manuscript Submission Form](#).

In addition to completing the Manuscript Submission Form, all submitted papers must include a conflict-of-interest statement for all authors in the Acknowledgments section. If authors have no relevant conflict of interest to disclose, this should be indicated in the Acknowledgments section.

Relevant conflict of interest (or lack thereof) should also be disclosed in the authors' comments to the editor during the submission process.

4.5. Color Figure Approval. For a manuscript that contains color figures and is accepted for publication, the corresponding author must complete a color printing approval form. Forms are available online through the manuscript submission process. The cost of printing in color, to be borne by the author, is \$490 U.S. per color figure. Color fees are based on individual figures as a whole, not by the part, i.e., A, B, C, etc. Authors will receive an invoice for publication fees when page proofs become available.

5. MANUSCRIPT CATEGORIES

See Section 6, [Manuscript Format and Style](#), for detailed instructions on formatting documents.)

5.1. Original Articles. Original Articles should be arranged in the following order: title page, structured abstract, introduction (no heading), "Research Design and Methods," "Results," "Conclusions," "Acknowledgments," "References," tables, and figure legends.

A **structured abstract** is required for all Original Articles and Brief Reports.

An abstract for an Original Article should not exceed 250 words. (This is not to be confused with abstracts submitted to the Annual Scientific Meeting, for which the word limit is higher.) The abstract must be self-contained and clear without reference to the text and should be written for a general journal readership. The abstract format should include four sections: “Objective” (the purpose or hypothesis of study), “Research Design and Methods” (the basic design, setting, number of participants and selection criteria, treatment or intervention, and methods of assessment), “Results” (significant data found), and “Conclusions” (the validity, limitations, and clinical applicability of the study and its results).

As of July 1, 2011 the journal will follow new formatting guidelines for new submissions: The **word count limit** for Original Articles is a maximum of 4,000 words. In addition, an original article is limited to a total combination of 4 tables and figures. Do not count words in tables, table legends, figure legends, title page, acknowledgments or references. **References** are limited to 40 citations. Exception to the word/table/figure/reference limit is rare.

A conflict-of-interest statement for all authors must be included in the main document, following the text, in the Acknowledgments section. If authors have no relevant conflict of interest to disclose, it should be indicated in the Acknowledgments section.

In the case of **multicenter studies**, authors should provide a list of participating investigators as an appendix to the paper. Papers will not be reviewed if this information is not included.

Where appropriate, **clinical and epidemiological studies** should be analyzed to see if there is an effect of sex or ethnicity. If there is no effect, it should be stated as such in the “Results” section.

Randomized Clinical Trial reporting: Authors of reports on randomized controlled trials are required to use the instructions and checklist in the [Consolidated Standards of Reporting Trials \(CONSORT\) Statement](#). The instructions and checklist are designed to ensure that information pertinent to the trial is included in the study report. CONSORT information may be included in a supplemental online-only file so that it does not affect word count limitations.

All **clinical trials** submitted to *Diabetes Care* for consideration of publication must be registered with a clinical trial registry approved by the International Committee of Medical Journal Editors (ICMJE). Please see Section 2.5 for more information.

5.2. Brief Reports. A Brief Report can be formatted in one of two ways:

As a clinical observation/research report consisting of a structured abstract stating the study's objectives, followed by a short introduction (2–3 sentences) and four concise sections: "Research Design and Methods," "Results," "Conclusions," and "References."

As a case report/case study consisting of a structured abstract, followed by a short introduction (2-3 sentences) and four sections: "History and Examination" describes the patient and provides a brief history; "Investigation" discusses the treatment findings and results; "Conclusions" summarizes the importance of the findings/results in one or two paragraphs; and "References."

Neither format should exceed the allowed word count limit. (See Section 6, “Manuscript Format and Style,” for further information.)

Brief Reports must **include a structured abstract** and may contain either one table or one figure, but not both.

The **format** of title page, margins, text, table, figure, and font size for a Brief Report is the same as for an Original Article. Manuscripts should be double-spaced, written in Arial or Times New Roman 12-point font, and saved as a .doc, .txt, or .rtf file. The figure or table must follow guidelines provided in Sections 6.2 and 6.3 of “Manuscript Format and Style.”

Brief Reports should include no more than **15 references**.

A **structured abstract** for a Brief Report should not exceed 150 words. The **word limit** for the main text is 1,000 words. Do not count words in the tables, figures, legends, the title page, acknowledgments, or references.

The abstract must be self-contained and clear without reference to the text and should be written for a general journal readership. The abstract format should include four sections that reflect the section headings in the main text.

A conflict-of-interest statement for all authors must be included in the main document, following the text, in the Acknowledgments section. If authors have no relevant conflict of interest to disclose, it should be indicated in the Acknowledgments section.

5.3. Letters to the Editor. All Letters to the Editor are published only in the online version of *Diabetes Care*. Online-only letters are still listed in the table of contents of the print version and will be assigned an "E" page number, but they should be cited by use of their DOI (digital object identifier) rather than a page number (e.g., 10.2337/dc07-XXXX).

Letters do not have abstracts, should not exceed 500 words (excluding a maximum of 5 references), and do not have tables or figures. As with all submissions, letters should be double-spaced and include a title page.

A Comment Letter is a letter that comments on a recently published article and should include the cited paper as reference 1 in the reference list. It should be submitted within 3 months of the article’s printed publication.

A Response Letter is an invited letter from the cited author that replies to the comment letter and must include the comment letter as reference 1 in the reference list.

All letters require a signed Manuscript Submission Form from the authors. This must be faxed or uploaded to the manuscript submission system at the time of submission, without exception. A conflict-of-interest statement for all authors must be included in the main document, following the text, in the Acknowledgments section. If authors have no relevant conflict of interest to disclose, it should be indicated in the Acknowledgments section.

5.4. Commentaries. *Diabetes Care* publishes Commentaries by invitation only. Commentaries normally accompany an original article or brief report and are invited by the editors. They should include a title page as with any submission, use 12-point Arial or Times New Roman font, and be double-spaced. A commentary is limited to 1200 words and 25 references. It does not have an abstract. As with all submission, it should a formatted title page. Signed Manuscript Submission Forms are required,

including a conflict-of-interest statement for all authors in the main document. This should be placed at the end of the text, in the Acknowledgments section. If the authors have no relevant conflict of interest to declare, it should be indicated in the Acknowledgments section.

5.5. Review Articles. Review Articles are by invitation or pre-approved submission. If you would like to submit an uninvited review, you must first submit a proposal to the editors.

The proposal should include: 1) a detailed outline of the content of the proposed review; 2) a general idea of the amount of original literature to be summarized; and 3) the background of the author(s) and a description of expertise in the area to be discussed in the review (or commentary). It is anticipated that the author(s) will have worked and published in the area covered by the review. The author should also state why he/she feels this particular review is suited for *Diabetes Care* and why the review would appeal to the readership.

Lastly, the authors must disclose whether they propose to write the entire article themselves, whether they received any form of sponsorship or honorarium for the material, and whether a pharmaceutical company, or its representative, was involved in the funding or authorship. In addition, the authors must point out any potential conflict of interest with a company whose products will be discussed in the review. All proposals should be submitted by e-mail (as Word document attachments) to Lyn Reynolds in the Editorial Office (lreynolds@diabetes.org). Proposals must be received by the first Wednesday of the month in order for it to be scheduled for discussion at the next editorial meeting (second Monday of each month) by the Editor and Associate Editors. Review Articles submitted without prior approval or invitation will be returned. All Review Articles (whether invited or by query) are subject to peer review.

Once approved, Review Articles are limited to 5000 words and 40-60 references. Review Articles do not have abstracts.

5.6 Editorials. Editorials are solicited by the Editorial Committee. As with all submissions, an editorial must include a title page and authors must provide a signed Manuscript Submission Form. The word limit for an Editorial is 1,500 words, not including references. Editorials normally do not contain figures or tables. A **conflict-of-interest statement** for all authors should be included at the end of the text or the Acknowledgments section, if one is included. Please label this section “Disclosure.” If the authors have no relevant conflict of interest to disclose, please indicate so in this section.

5.7. Supplements. Supplements must be approved prior to submission. A proposal for a supplement should first be submitted to the Publications Department of the ADA (ckohler@diabetes.org) and must specify the following:

The name of the organization(s) sponsoring and funding the supplement (not merely the name of the public relations agency handling its publication).

If the supplement is based on a symposium, where and when the symposium was held and how the speakers and papers were selected.

Whether authors will be paid and, if so, how much.

If the proposal is approved, it will be forwarded to the Editor of *Diabetes Care*. Initial approval by the ADA does not commit the Editor to accept a proposal in whole or part. All manuscripts are subject to the same peer review as other manuscripts in the journal.

For complete instructions on submitting a supplement, please contact the [Editorial Office](#).

6. MANUSCRIPT FORMAT AND STYLE: Articles must be in clear and understandable English. Non-native English authors are encouraged to seek the assistance of an English-proficient colleague, or a communications agency such as [“American Journal Experts”](#), to help improve the clarity and readability of a paper before it is submitted to the journal.

6.1. The Main Document includes the title page, abstract, main text, acknowledgements, disclosure, figure legends, references, and tables. Please do not use headers, footers, or endnotes in your paper.

6.1.1 Text Composition. Articles should be written in clear, concise English following the recommendations for scientific writing found in *Scientific Style and Format*, the Council of Science Editors (CSE) style manual (7th ed., 2006, Reston, VA, Council of Science Editors). All accepted manuscripts will be edited according to the CSE style manual and *The Chicago Manual of Style* (15th ed., 2003, Chicago, IL, The University of Chicago Press) by ADA professional publications staff. The authors are responsible for all statements made in their articles or editorials, including any editing changes made by staff. Proof pages should be read carefully. The designations *type 1 diabetes* and *type 2 diabetes* should be used when referring to the two major forms of diabetes. Abbreviations for diabetes, such as T2D for *type 2 diabetes*, should not be used. The term *diabetic* should not be used as a noun. All manuscripts should be double-spaced, in Arial or Times New Roman 12-point font, and saved as a .doc, .txt, or .rtf file. In addition, please do not "lock" or "page protect" your document, and avoid using footnote and endnote functions.

6.1.2. Abbreviations and Units. Abbreviations should be used only when necessary, e.g., for long chemical names (HEPES), procedures (ELISA), or terms used throughout the article. See the [list of abbreviations](#) that need not be defined; all others must be defined at first use. Abbreviate units of measure only when used with numbers. Abbreviations may be used in tables and figures. The CSE style manual contains lists of standard scientific abbreviations.

Clinical laboratory values and units should be in [Système International \(SI\)](#) form. Kilocalories should be used rather than kilojoules. Glycated hemoglobin should be expressed as percentage of total and as standard deviation from mean control levels.

6.1.3. Materials. Authors should provide the name and location (city and state/country) of the source for specified chemicals and other materials only if alternate sources are considered unsatisfactory.

6.1.4. Title Page. Every manuscript, including Letters and Brief Reports, must have an accompanying title page. The title page should include the title; a short running title (less than 47 characters and spaces combined); the first name, middle initial, last name, and highest academic degree of each author; affiliation (in English) of each author during the study being reported; name, current address, telephone number, fax number, and e-mail address of the corresponding author; and the word count and number of tables and figures.

The Main Document should be in Word document format (not as a PDF). This will allow our Editorial Office to verify the word count and our production staff to turn your paper (if accepted) into an article.

6.1.5. **Font.** Text, including title and author names, should be in 12-point Arial or Times New Roman. Please avoid using boldface font. Text in tables should be no smaller than 10-point font.

6.1.6. **Margins.** Margins should be 1" at the top and bottom and 1" on the left and right sides.

6.1.7. **Section Headers.** Except for the Abstract, new sections should not begin on new pages. Each new section should immediately follow the end of the previous section. See [Manuscript Categories](#) for the proper headings.

6.1.8. **Abstract.** Please see Section 5.1.1 of [Manuscript Categories](#).

6.1.9. **Word Count Limit.** Please see instructions for the individual type of article being submitted under section 5.1.2 of [Manuscript Categories](#).

6.1.10. **Acknowledgments.** The acknowledgments are located after the main text and before the reference list. Acknowledgments should contain the author contributions paragraph, brief statements of assistance, the guarantor's name (person(s) taking responsibility for the contents of the article), funding/financial support, and reference to prior publication of the study in abstract form, where applicable.

6.1.11. **References.** The reference list should go at the end of the document, after the main text and acknowledgments (if applicable) and before the tables. Original Articles are limited to 40 references. Brief Reports are allowed 15 references. Letters are allowed 5 references. Review Articles are allowed 40-60 references and a Meta-analysis should have no more than 40 references.

Reference numbers in the text should appear in chronological order in normal type and in parentheses [e.g., "In the study by Norton et al. (23)..."]. Please do not use the footnote or endnote function to cite studies or create a reference list. A reference manager must have the ability to customize the display of references. For example, the reference application should have the option to list the references at the end of the paper, as opposed to listing the references as endnotes or footnotes at the bottom of each page, and should not embed the list in the text as a series of endnotes/footnotes. When using a reference manager (e.g., Thomson's EndNote Reference Program), don't forget to generate the list as a bibliography in a style suitable to *Diabetes Care*, and then save and submit as the final step to creating the references. Otherwise, references should be manually inserted.

All authors must be listed by first initials and last name in each reference, and please provide inclusive page numbers. Journal titles should be abbreviated according to the National Library of Medicine's [List of Journals Indexed for Medline](#); for unlisted journals, please provide complete journal titles. Material in press may be cited, but copies of such material may be requested. Authors are responsible for the accuracy of the references. Click [here](#) for examples of how references should be formatted.

6.1.12. **Supplemental Data.(Original Articles only)** Original Articles may contain online supplemental files if necessary. All supplementary data to appear online-only file should be combined in one document file (whenever possible) and uploaded separately during the submission process. It must be clearly labeled as "**Online-Only Supplemental Material.**"

All online-only files are subject to review. Content of files submitted for online use only will *not* be copyedited. As such, please review the information carefully before

submitting. In addition, supplemental Online-only material *must* be referenced in the text at least once (e.g., “Supplemental Table S1”)

Lists that include names of **principal investigators or writing groups** may be included in print as an Acknowledgement if no more than 150 words and should not be counted in the word count.

Note: Please include a comment to the editor justifying the necessity of online supplemental materials for your Original Article. Allowance of online supplemental materials is at the discretion of the Editorial Committee.

Do not put online supplemental material in the main document. Instead, it should be uploaded as a separate document.

6.2. Tables. Each table should be inserted on a separate page at the end of the document with the table number, title, and legend indicated. Table legends should be inserted below the table and not be included inside the table. Tables should be created using Word and the "Insert Table" command. Please use Arial or Times New Roman font, no smaller than 10-point. Tables with internal divisions are not allowed (Tables 1A and B) and should be submitted as individual tables (Tables 1 and 2).

6.3. Figures. *Diabetes Care* uses digital publishing methods throughout the journal production process. If your article is accepted, it will be published both in the printed journal and online. The following sections provide information on how to format your figures to ensure the best possible reproduction of your images.

Size. Figures should be produced at the size they are to appear in the printed journal. Please make sure your figures will fit in one, two, or three columns in width. Multi-paneled figures should be assembled in a layout that leaves the least amount of blank space.

1 column = 13 picas wide, 2.2 in, 5.6 cm

2 columns = 28 picas wide, 4.6 in, 11.7 cm

3 columns = 41 picas, 6.8 in, 17.3 cm

Font. At 100% size, fonts should be 8-10 points and used consistently throughout all figures.

Text. Information on the axes should be succinct, using abbreviations where possible, and the label on the y-axis should read vertically, not horizontally. Key information should be placed in any available white space **within** the figure; if space is not available, the information should be placed in the legend. In general, figures with multiple parts should be marked A, B, C, etc., with a description of each panel included in the legend rather than on the figure.

Line and bar graphs. Lines in graphs should be bold enough to be easily read after reduction, as should all symbols used in the figure. Data points are best marked with the following symbols, again assuring that they will be readily distinguishable after reduction: ○ ● □ ■ △ ▲. In the figure legend, please use words rather than the symbols; e.g., "black circles = group 1; white squares = group 2; black bars = blood glucose; white bars = C-peptide." Bars should be black or white only, unless more than two datasets are being presented; additional bars should be drawn with clear bold hatch marks or stripes, **not** shades of gray.

Line or bar graphs or flow charts with text should be created in black and white, **not** shades of gray, which are difficult to reproduce in even tones.

Formatting digital figures files for print and online reproduction. To meet ADA’s quality standards for publication, it is important to submit digital art that conforms to the appropriate resolution, size, color mode, and file format. Doing so

will help to avoid delays in publication and maximize the quality of images, both online and in print. Please refer to [ADA's Digital Art Guidelines](#) when preparing your files. If you are unable to provide files that meet the specifications outlined in the Guidelines, you may submit your original source files (files from the program in which they were originally created).

Reproductions. If materials (e.g., figures and/or tables) are taken from other sources, the author must provide written permission for reproduction from the original publisher and author at the time of submission. In addition, the source should be cited at the end of the figure legend.

Digital image manipulation. The American Diabetes Association has adopted the statement developed by the [Journal of Cell Biology](#) as its policy on the manipulation of digital images:

“No specific feature within an image may be enhanced, obscured, moved, removed, or introduced. The grouping of images from different parts of the same gel, or from different gels, fields, or exposures must be made explicit by the arrangement of the figure (i.e., using dividing lines) and in the text of the figure legend. Adjustments of brightness, contrast, or color balance are acceptable if they are applied to the whole image and as long as they do not obscure, eliminate, or misrepresent any information present in the original, including backgrounds. Without any background information, it is not possible to see exactly how much of the original gel is actually shown. Non-linear adjustments (e.g., changes to gamma settings) must be disclosed in the figure legend.”

All digital images in manuscripts accepted for publication will be scanned using image forensics software for any indication of improper manipulation. Cases of questionable or inappropriate image alterations will be referred to the Association’s Subcommittee on Ethical Scientific Publications (ESP). The ESP may request the original data from the authors for comparison to the prepared figures. If the authors fail to provide the original data, the acceptance of the manuscript will be revoked. Cases of deliberate misrepresentation of data will result in revocation of acceptance, and will be reported to the corresponding author's home institution and/or funding agency as appropriate.

For examples of what constitutes improper digital manipulation (as well as other forms of scientific misconduct), ADA encourages authors to refer to the 2006 editorial by the *Journal of Clinical Investigation* titled “[Stop Misbehaving!](#)” In addition, authors are encouraged to refer to [Adobe’s white paper](#) on using Photoshop CS3 Extended in biomedical imaging. The paper provides useful information on maintaining image integrity, editing nondestructively, and the medical and scientific image workflow.

7. SUBMITTING A MANUSCRIPT

Please read the complete instructions for authors before submitting your manuscript to *Diabetes Care* via <http://mc.manuscriptcentral.com/diabetescare>.

Your manuscript should be submitted under the **user account** of the designated **corresponding author** (the contact person listed on the title page of the manuscript). If the corresponding author does not have a user account, please follow the instructions on the submission site. *Please allow 24-48 hours for a user account to be created.*

Useful Tips:

In the File Upload Center, you will be able to browse your computer for the files associated with your manuscript. When you upload each file, be sure to choose a designation from a pull-down menu that describes the file content (e.g., “Main Document,” “Figure,” “Table,” etc.). In addition, please make sure each file name clearly describes its content (e.g., “figure1.jpg,” “table2.doc,” “coverletter.doc,” etc.).

The system automatically converts files to PDF files. Please do not upload PDF files except for signed Manuscript Submission Forms. Also, please do not upload zip files, docx or pptx files.

A Instructions for submitting revised manuscript are included in the initial decision letter; revisions must meet all formatting requirements and word limits; no exceptions will be made. In addition, all signed manuscript forms must be faxed to the Editorial Office by the time the revision is submitted. If complete forms have not been received, it is likely that the revision will be unsubmitted. Receipt of forms may be verified by contacting Joan Garrett (jgarrett@diabetes.org).

Revisions should be created by selecting “manuscripts with decisions” from the Author Center menu. Find the manuscript to be revised in the manuscript list. Click “create a revision” in the right column and a revision file will be created automatically. Revisions submitted under a new manuscript number will be returned to the author for proper submission.

When revising your manuscript, please show corrections by track changes or a colored font to show additions and strikeout to show deleted text. Be sure to respond to all reviewer comments on the original submission.

If you are submitting a revision, please include only the latest set of files. If you have updated a file, upload only the revised file. Do not include originally submitted files. Figures and tables must be uploaded with each version. **Important:** If it is a second or third revision, please indicate that the previously converted figures from the first revision are acceptable and may be used for print production if accepted.

Once your text and image files are uploaded, please view these files to ensure they appear legibly and that all special characters have translated properly. Do not click "Submit Manuscript" until you are satisfied with the quality of the proofs. If you are having trouble uploading files, please click on the “Help” button in the top right corner of the manuscript submission screen or contact the [Editorial Office](#) for guidance.

8. ACCEPTED MANUSCRIPTS

8.1. **Prepublication.** For detailed information on publish-ahead-of-print articles, see Section 2.2 of [Policies](#).

8.2. Accepted manuscripts will be scheduled for publication as soon as possible.

The designated corresponding author will receive notification of availability of page proofs by e-mail. Corrections should be returned within 24 hours of receipt of the proof. Failure to do so may delay the publication of the article.

Correspondence concerning the copyediting and proofreading of accepted manuscripts should be addressed to Valentina Such, Editorial Manager, Diabetes Care, American Diabetes Association, 1701 North Beauregard St., Alexandria, VA 22311; tel: 703-299-2083; fax: 703-253-4870; e-mail: vsuch@diabetes.org.

Correspondence concerning the production of accepted articles and availability of page proofs should be addressed to Amy Gavin, Production Editor, American Diabetes Association, 1701 North Beauregard St., Alexandria, VA 22311; tel: 703-299-2033; fax 703-253-4870; e-mail:agavin@diabetes.org.

9. FINANCIAL OBLIGATIONS

Page charges are assessed for Original Articles and Brief Reports to help defray costs of publication. The charge is \$90 per page. As noted under [Color Figure Approval](#) (*Section 4.5.*), each color figure printed will incur a charge of \$490. The corresponding author will receive via e-mail a pro forma invoice, as well as a reprint order form, when page proofs become available. Unless otherwise indicated, ADA will assume that the corresponding author is taking responsibility for payment.

Updated June 1, 2011

Appendix 3

STROBE Guidelines

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in

		the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(b) Report category boundaries when continuous variables were categorized
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

Appendix 4

Systematic review search results

Search Journals Books My Workspace

Search History (15 searches) (Click to close) View Saved

<input type="checkbox"/>	# ▲	Searches	Results	Search Type	Actions
<input type="checkbox"/>	1	Stress Disorders, Post-Traumatic/	18265	Advanced	Display More >
<input type="checkbox"/>	2	limit 1 to (humans and yr="2000 - 2012")	13207	Advanced	Display More >
<input type="checkbox"/>	3	Anxiety/	46772	Advanced	Display More >
<input type="checkbox"/>	4	limit 3 to (humans and yr="2000 - 2012")	19315	Advanced	Display More >
<input type="checkbox"/>	5	Depression/	66133	Advanced	Display More >
<input type="checkbox"/>	6	limit 5 to (humans and yr="2000 - 2012")	34757	Advanced	Display More >
<input type="checkbox"/>	7	2 or 4 or 6	58532	Advanced	Display More >
<input type="checkbox"/>	8	Intensive Care/	13780	Advanced	Display More >
<input type="checkbox"/>	9	limit 8 to (humans and yr="2000 - 2012")	9265	Advanced	Display More >
<input type="checkbox"/>	10	Critical Care/	23111	Advanced	Display More >
<input type="checkbox"/>	11	limit 10 to (humans and yr="2000 - 2012")	9580	Advanced	Display More >
<input type="checkbox"/>	12	Intensive Care Units/	31253	Advanced	Display More >
<input type="checkbox"/>	13	limit 12 to (humans and yr="2000 - 2012")	17769	Advanced	Display More >
<input type="checkbox"/>	14	9 or 11 or 13	33091	Advanced	Display More >
<input type="checkbox"/>	15	7 and 14	316	Advanced	Display More >

Remove Selected Save Selected | Combine selections with:

Save Search History RS3

Search History (15 searches) (Click to close)						View Saved
<input type="checkbox"/>	# ▲	Searches	Results	Search Type	Actions	CONTRACT
<input type="checkbox"/>	1	posttraumatic stress disorder/	28868	Advanced	Display More >	
<input type="checkbox"/>	2	limit 1 to (human and yr=2000 - 2012*)	20843	Advanced	Display More >	
<input type="checkbox"/>	3	anxiety/	95176	Advanced	Display More >	
<input type="checkbox"/>	4	limit 3 to (human and yr=2000 - 2012*)	46076	Advanced	Display More >	
<input type="checkbox"/>	5	depression/	214326	Advanced	Display More >	
<input type="checkbox"/>	6	limit 5 to (human and yr=2000 - 2012*)	123882	Advanced	Display More >	
<input type="checkbox"/>	7	intensive care/	70610	Advanced	Display More >	
<input type="checkbox"/>	8	limit 7 to (human and yr=2000 - 2012*)	34715	Advanced	Display More >	
<input type="checkbox"/>	9	intensive care unit/	66815	Advanced	Display More >	
<input type="checkbox"/>	10	limit 9 to (human and yr=2000 - 2012*)	46525	Advanced	Display More >	
<input type="checkbox"/>	11	critical care.mp.	25320	Advanced	Display More >	
<input type="checkbox"/>	12	limit 11 to (human and yr=2000 - 2012*)	14777	Advanced	Display More >	
<input type="checkbox"/>	13	2 or 4 or 6	165407	Advanced	Display More >	
<input type="checkbox"/>	14	8 or 10 or 12	80543	Advanced	Display More >	
<input type="checkbox"/>	15	13 and 14	1243	Advanced	Display More >	



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Print Search History Retrieve Searches Retrieve Alerts Save Searches / Alerts				
<input type="checkbox"/> Select / deselect all <input type="button" value="Search with AND"/> <input type="button" value="Search with OR"/> <input type="button" value="Delete Searches"/> <input type="button" value="Refresh Search Results"/>				
Search ID#	Search Terms	Search Options	Actions	
<input type="checkbox"/> 59	S4 and 58	Search modes - Boolean/Phrase	View Results (264)	View Details Edit
<input type="checkbox"/> 58	S5 or S6 or 57	Search modes - Boolean/Phrase	View Results (59002)	View Details Edit
<input type="checkbox"/> 57	intensive care unit	Search modes - Boolean/Phrase	View Results (15215)	View Details Edit
<input type="checkbox"/> 56	intensive care	Search modes - Boolean/Phrase	View Results (36937)	View Details Edit
<input type="checkbox"/> 55	critical care	Search modes - Boolean/Phrase	View Results (30475)	View Details Edit
<input type="checkbox"/> 54	S1 or S2 or 53	Search modes - Boolean/Phrase	View Results (31520)	View Details Edit
<input type="checkbox"/> 53	(MM "Depression")	Limiters - Published Date from: 20000101-20111231; English Language Search modes - Boolean/Phrase	View Results (23221)	View Details Edit
<input type="checkbox"/> 52	(MM "Anxiety")	Limiters - Published Date from: 20000101-20111231; English Language Search modes - Boolean/Phrase	View Results (4980)	View Details Edit
<input type="checkbox"/> 51	(MM "Stress Disorders, Post-Traumatic")	Limiters - Published Date from: 20000101-20111231; English Language Search modes - Boolean/Phrase	View Results (5404)	View Details Edit



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Search History/Alerts					
Print Search History Retrieve Searches Retrieve Alerts Save Searches / Alerts					
<input type="checkbox"/> Select / deselect all		<input type="button" value="Search with AND"/>	<input type="button" value="Search with OR"/>	<input type="button" value="Delete Searches"/>	<input type="button" value="Refresh Search Results"/>
Search ID#	Search Terms	Search Options	Actions		
<input type="checkbox"/> 59	S7 and S8	Search modes - Boolean/Phrase	View Results (158)	View Details	Edit
<input type="checkbox"/> 58	S4 or S5 or S6	Search modes - Boolean/Phrase	View Results (5065)	View Details	Edit
<input type="checkbox"/> 57	S1 or S2 or S3	Search modes - Boolean/Phrase	View Results (32275)	View Details	Edit
<input type="checkbox"/> 56	intensive care unit	Limiters - Published Date from: 20000101-20121231; English Search modes - Boolean/Phrase	View Results (2672)	View Details	Edit
<input type="checkbox"/> 55	critical care	Limiters - Published Date from: 20000101-20121231; English Search modes - Boolean/Phrase	View Results (2631)	View Details	Edit
<input type="checkbox"/> 54	DE "Intensive Care"	Limiters - Published Date from: 20000101-20121231; English Search modes - Boolean/Phrase	View Results (1710)	View Details	Edit
<input type="checkbox"/> 53	DE "Depression (Emotion)"	Limiters - Published Date from: 20000101-20121231; English Search modes - Boolean/Phrase	View Results (4114)	View Details	Edit
<input type="checkbox"/> 52	DE "Anxiety"	Limiters - Published Date from: 20000101-20121231; English Search modes - Boolean/Phrase	View Results (17012)	View Details	Edit
<input type="checkbox"/> 51	DE "Posttraumatic Stress Disorder"	Limiters - Published Date from: 20000101-20121231; English Search modes - Boolean/Phrase	View Results (12708)	View Details	Edit

Appendix 5

NHS North of Scotland Research Ethics Committee Approval

NRES Committees - North of Scotland

Summerfield House
2 Eday Road
Aberdeen
AB15 6RE

Telephone: 01224 558474
Facsimile: 01224 558609
Email: nosres@nhs.net



03 August 2011

Miss Kirsty Matheson
Trainee Clinical Psychologist
NHS Grampian
c/o Psycho-Oncology
Roxburghe House
Ashgrove Road
ABERDEEN
AB25 3AE

Dear Miss Matheson

Study title: Emotional wellbeing following hospital admission for diabetic ketoacidosis
REC reference: 11/AL/0339

Thank you for your letter of 02 August 2011, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information was considered by the Scientific Officer.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at <http://www.rdforum.nhs.uk>.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	Version	Date
Covering Letter		22 July 2011
Covering Letter		01 August 2011
Investigator CV	n/a	06 June 2011
Other: Care protocol	1	30 May 2011
Other: CV - David Gillanders	n/a	02 March 2011
Other: CV - Andrew Keen	n/a	06 June 2011
Other: Participant covering letter time 2 3 & 4	1	30 May 2011
Other: Participant follow up letter time 3 & 4	1	30 May 2011
Other: GP Letter Time 1	1	30 May 2011
Other: GP Letter Time 3	1	30 May 2011
Other: GP Letter Time 4	1	30 May 2011
Other: Attachment to questionnaires at Time 4	1	30 May 2011
Other: Post-traumatic stress: key facts from the Royal College of Psychiatrists	n/a	06 June 2011
Other: Booklet - Depression	n/a	30 November 2009
Other: Booklet - Health Psychology at the Diabetes Centre	n/a	30 November 2009
Other: Booklet - Anxiety	n/a	30 November 2009
Other: Recruitment Protocol	2	22 July 2011
Other: Participant Reminder Letter	1	01 August 2011
Participant Consent Form	2	22 July 2011
Participant Information Sheet	3	01 August 2011
Protocol	3	01 August 2011
Questionnaire: HADS	1	30 May 2011
Questionnaire: Impact of Event Scale - Revised	1	30 May 2011
Questionnaire: PAID	1	30 May 2011
Questionnaire: Acceptance & Action (AAQ-11)	1	30 May 2011
Questionnaire: CFQ15	1	30 May 2011
Questionnaire: NOVEL	1	30 May 2011
REC application		09 June 2011
Response to Request for Further Information		27 July 2011

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.

After ethical reviewReporting requirements

The attached document "*After ethical review – guidance for researchers*" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

11/AL/0339**Please quote this number on all correspondence**

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

Yours sincerely

Professor Siladitya Bhattacharya
Chair

Copy to: Miss Gemma Watson
NHS Grampian R&D Department

Appendix 6

Participant Information Sheet

Participant Information Sheet
V3 – 01.08.11

Emotional Wellbeing following admission for diabetic ketoacidosis

You are being invited to participate in this project because you have recently experienced diabetic ketoacidosis.

Before you decide, it is important for you to understand why the research is being carried out and what participating will involve. Please take time to read the following information carefully and discuss it with others if you wish. Please ask us if there is anything that is not clear or if you would like more information. Thank you for reading this.

What is the background to the study?

We know from research conducted over the past few decades that critical medical events can have a substantial impact on emotional wellbeing and this often goes undetected. Many of those who report clinically significant levels of emotional problems following traumatic events make a good recovery without the need for treatment. However, for a substantial minority, the negative emotional impact is lasting.

The emotional wellbeing of people with diabetes is especially important. This is because emotional wellbeing is closely related to diabetes control and diabetes control largely dictates the longer-term health outcomes for people with diabetes.

Diabetic ketoacidosis is a critical medical event, however little is known about its long term psychological consequences. Therefore, by taking measurements of psychological wellbeing and engagement with diabetes will supply health professionals with information to provide a more effective follow up care pathway following diabetic ketoacidosis.

What is the purpose of the study?

The purpose of the study is to measure the emotional wellbeing of those with type 1 diabetes after an admission to hospital for diabetic ketoacidosis. This will then inform future care provision and identify vulnerability factors for those who experience this complication.

Why have I been chosen?

You have recently experienced diabetic ketoacidosis and were admitted to hospital to manage this complication of type 1 diabetes.

Do I have to take part?

No. It is up to you whether or not you take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time without giving a reason for your withdrawal from the study.

What will happen to me if I take part?

You will be asked to complete a set of questionnaires at 3 different time points. Initially you will be provided the questionnaires during your current admission. You will be asked to complete and return them in the enclosed stamped address envelope within 1 week of receiving them.

The same questionnaire shall be posted out to you one month, three months and six months later. Once you have completed these questionnaires, you will be asked to return them in the stamped address envelope provided. Should you not return the questionnaires within one week, the investigator shall send out a letter to remind you. You will also be asked your consent for the primary investigator to access your medical records and routinely collected data from the diabetes centre.

What do I have to do?

If you would like to take part in the study, you can contact the researcher, Kirsty Matheson, who will provide you with a set of questionnaires to complete. You will be asked to read and sign a consent form prior to commencement of the study. The researcher will be present in your hospital to answer any questions about the study.

What are the possible benefits of taking part?

There are no direct benefits. However, you are being given the opportunity to contribute to the improved understanding of how diabetic ketoacidosis may impact the emotional wellbeing of those with type 1 diabetes.

Will my taking part in this study be kept confidential?

Yes. All information collected from you during the course of this study will be kept strictly confidential. Participants will be assigned a participant number and individual data will not be reported in outputs from the study.

What will happen to the results of the research study?

The results of the study will be used to evaluate emotional wellbeing of those with type 1 diabetes post diabetic ketoacidosis. Results will be submitted to a diabetes care journal for publication.

Who has reviewed the study?

The study has been reviewed by NRES Committees- North of Scotland.

Contact for further information

If you have any questions about the study please contact Kirsty Matheson, Trainee Clinical Psychologist; e: kirsty.matheson@nhs.net or tel: 01224 552706.

Independent contact

If you wish to contact an independent about research in general or have any cause to complain regarding this project please contact: Dr. Heather Wilkinson, Research Director, School of Health in Social Science, University of Edinburgh, Teviot Place, Edinburgh, EH8 9AG. Tel: 0131 651 3969.

To report problems with the study

For enquiries about complaints or to make a complaint about the study please contact:

NHS Grampian Complaints Team

Westholme

Woodend Hospital

Queens Road

Aberdeen

AB15 6LS

Telephone: 01224 556447

Thank you for reading this.

Appendix 7

Participant Consent Form

Patient Identification Number for this trial:

CONSENT FORM

V 2

22.07.11

Title of Project: Emotional wellbeing following hospital admission for diabetic ketoacidosis

Name of Researcher: Kirsty Matheson

Please initial box

1. I confirm that I have read and understand the information sheet dated 01.08.11 (version 3) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

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

3. I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.

4. I agree to the primary investigator accessing medical records and routinely collected diabetes related data from the SCI-DC database.

5. In the event that I lose the capacity to make decisions my data can still be used.

6. I agree to my GP being informed of my participation in the study.

7. I agree to take part in the above study.

_____	_____	_____
Name of Patient	Date	Signature

_____	_____	_____
Name of Person Taking Consent	Date	Signature

When completed: 1 for participant; 1 for researcher site file; 1 (original) to be kept in medical notes.

Appendix 8

Letter to GP and diabetes team regarding patient participation

**Grampian Diabetes
Managed Clinical Network**

Woolmanhill Hospital
Aberdeen
AB25 1LD

GP Name
GP Practice Address

Date
kirsty.matheson@nhs.net

Dear Colleague

Re: Participant Name (Date of Birth) Address, CHI

Your patient has agreed to take part in the following study “**Emotional wellbeing following hospital admission for diabetic ketoacidosis**”. A copy of the patient information sheet is enclosed for your information. As part of the study your patient may be identified as having significant levels of depression and/or anxiety and/ or post traumatic stress disorder symptoms. If your patient scores clinically significant for the aforementioned domains at 3 month follow up, I shall notify you.

If you require any further information please contact Kirsty Matheson, Trainee Clinical Psychologist by email (kirsty.matheson@nhs.net) or tel (01224 552706).

Yours sincerely

Kirsty Matheson
Trainee Clinical Psychologist

Dr Andrew Keen
Consultant Health Psychologist

CC: ARI Notes
 Diabetes Medical Notes
Enclosed: Information sheet

Appendix 9

Three month follow-up patient letter if scoring at clinical levels for anxiety/
depression/ PTSD

11/AL/0339 version 1 30/05/11
Participant follow up letter follow-up
letter if clinical levels

**Grampian Diabetes Managed
Clinical Network**

Woolmanhill Hospital
Aberdeen
AB25 1LD



Participant Name

Address

Date

Dear Participant

Thank you very much for recently completing the set of questionnaires for the study
“Emotional wellbeing following hospital admission for diabetic ketoacidosis”.

After scoring up the inventories you kindly filled out, your scores indicate that you are scoring at clinical significance for *anxiety/ depression/ post traumatic stress disorder symptoms (to delete as appropriate)*. At this time we would advise you to contact your General Practitioner (GP) to discuss this further. We shall also notify your GP of your self-report scores.

Please find enclosed a leaflet about *anxiety/ depression/ post traumatic stress disorder symptoms (to delete as appropriate)* as well as a leaflet about the psychology service at the diabetes centre (with contact details if you wish to refer yourself).

I appreciate that this letter may be of surprise to you and therefore please do not hesitate to contact me should you require any further information, email: kirsty.matheson@nhs.net or telephone 01224 552706.

Yours sincerely

Kirsty Matheson
Trainee Clinical Psychologist

Dr Andrew Keen
Consultant Health Psychologist

Enclosed: Appropriate leaflets

Appendix 10

Three month follow-up letter to GP if patient scoring at clinical levels for anxiety/
depression/ PTSD

**Grampian Diabetes
Managed Clinical Network**

Woolmanhill Hospital
Aberdeen
AB25 1LD



GP Name
GP Practice Address

Date

kirsty.matheson@nhs.net

Dear Colleague

Re: Participant Name (Date of Birth) Address, CHI

I wrote to you on the (date) to inform you that your patient had enrolled in the following study
“Emotional wellbeing following hospital admission for diabetic ketoacidosis”.

At three months follow-up your patient has scored at clinical significance for *anxiety/ depression/
post traumatic stress disorder symptoms (delete as appropriate)*.

I have informed your patient that they have scored at clinically significant levels and advised
them to contact you. In addition, I sent your patient an information leaflet about *anxiety/
depression/ post traumatic stress disorder symptoms (delete as appropriate)* as well as
information about the local diabetes psychology service (which has details for self-referral).

If you require any further information please contact Kirsty Matheson, Trainee Clinical
Psychologist by email (kirsty.matheson@nhs.net) or tel (01224 552706).

Yours sincerely

Kirsty Matheson
Trainee Clinical Psychologist

Dr Andrew Keen
Consultant Health Psychologist

CC: ARI Notes
 Diabetes Medical Notes

Enclosed: Patient letter
 Anxiety/ depression/ PTSD psycho-education
 NHS Grampian Diabetes Psychology Information leaflet

Appendix 11

Hospital Anxiety and Depression Scale (HADS)

HADS

This questionnaire will help you to let us know how you are. Read each item and tick the response that comes closest to how you have felt in the **last week**. Don't take too long over your replies, your immediate reaction will probably be more accurate than a long thought out response.

1^a. I feel tense or 'wound up'

- 3 Most of the time
- 2 A lot of the time
- 1 From time to time
- 0 Not at all

2^d. I still enjoy the things I used to enjoy

-
- 0 Definitely as much
- 1 Not quite so much
- 2 Only a little
- 3 Hardly at all

3^a. I get a sort of frightened feeling as if something awful is about to happen

-
- 3 Very definitely and quite badly
- 2 Yes, but not too badly
- 1 A little, but it doesn't worry me
- 0 Not at all

4^d. I can laugh and see the funny side of things

- 0 As much as I always could
- 1 Not quite so much now
- 2 Definitely not so much now
- 3 Not at all

5^a. Worrying thoughts go through my mind

- 3 A great deal of the time
- 2 A lot of the time
- 1 From time to time but not too often.
- 0 Only occasionally

6^d. I feel cheerful

- 3 Not at all
- 2 Not often
- 1 Sometimes
- 0 Most of the time

7^a. I can sit at ease and feel relaxed

- 0 Definitely
- 1 Usually
- 2 Not often
- 3 Not at all

8^d. I feel as if I am slowed down

- 3 Nearly all the time
- 2 Very often
- 1 Sometimes
- 0 Not at all

9^a. I get a sort of frightened feeling like 'butterflies' in the stomach

- 0 Not at all
- 1 Occasionally
- 2 Quite often
- 3 Very often

10^d. I have lost interest in my appearance

- 3 Definitely
- 2 I don't take so much care as I should
- 1 I may not take quite as much care
- 0 I take just as much care as ever

11^a. I feel restless as if I have to be on the move

- 3 Very much indeed
- 2 Quite a lot
- 1 Not very much
- 0 Not at all

12^d. I look forward with enjoyment to things

- 0 As much as ever I did
- 1 Rather less than I used to
- 2 Definitely less than I used to
- 3 Hardly at all

13^a. I get sudden feelings of panic

- 3 Very often indeed
- 2 Quite often
- 1 Not very often
- 0 Not at all

14^d. I can enjoy a good book or radio or TV programme

- 0 Often
- 1 Sometimes
- 2 Not often
- 3 Very seldom

A: 0-7 8-10 >10
D: 0-7 8-10 >10

Appendix 12

Impact of Events Scale - Revised (IES-R)

IMPACT OF EVENT SCALE – REVISED

Below is a list of difficulties people sometimes have after stressful life events. Please read each item, and then indicate how distressing each difficulty has been for you **DURING THE PAST SEVEN DAYS** with respect to **your recent hospital admission for diabetic ketoacidosis**, which occurred on _____.

How much were you distressed or bothered by these difficulties?

0 = Not at all; 1 = A little bit; 2 = Moderately; 3 = Quite a bit; 4 = Extremely.

1. Any reminder brought back feelings about it. _____
2. I had trouble staying asleep. _____
3. Other things kept making me think about it. _____
4. I felt irritable and angry. _____
5. I avoided letting myself get upset when I thought about it or was reminded of it. _____
6. I thought about it when I didn't mean to. _____
7. I felt as if it hadn't happened or wasn't real. _____
8. I stayed away from reminders of it. _____
9. Pictures about it popped into my mind. _____
10. I was jumpy and easily startled. _____
11. I tried not to think about it. _____
12. I was aware that I still had a lot of feelings about it, but I didn't deal with them. _____
13. My feelings about it were kind of numb. _____
14. I found myself acting or feeling like I was back at that time. _____
15. I had trouble falling asleep. _____
16. I had waves of strong feelings about it. _____
17. I tried to remove it from my memory. _____
18. I had trouble concentrating. _____
19. Reminders of it caused me to have physical reactions, such

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as sweating, trouble breathing, nausea, or a pounding heart.

20. I had dreams about it.

21. I felt watchful and on-guard.

22. I tried not to talk about it.

Total IES-R score

Appendix 13

Problem Areas in Diabetes (PAID)

PAID

Which of the following diabetes issues are currently problems for you? Circle the number that gives the best answer for you. Please answer all questions.

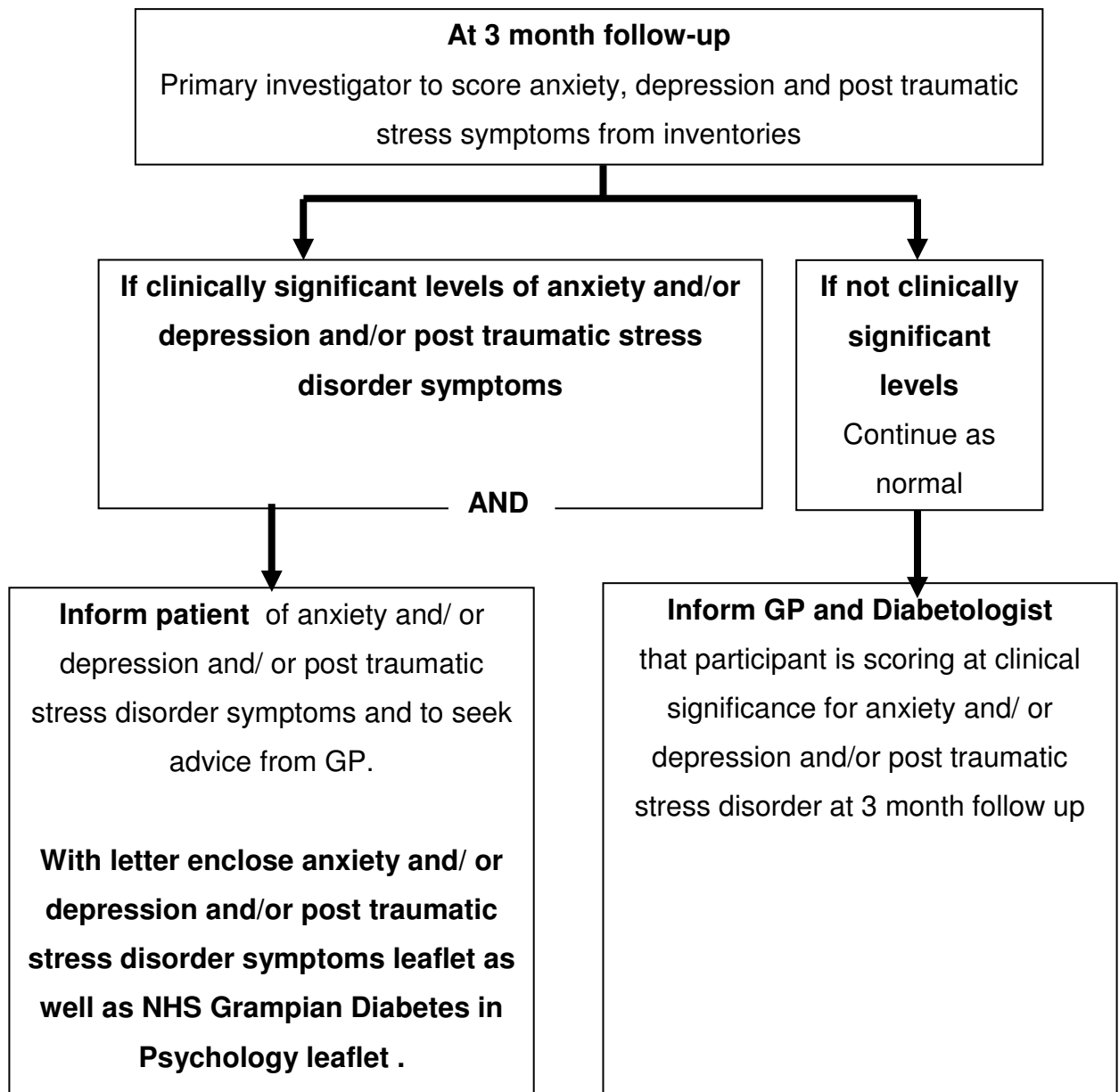
	Not a Problem	Minor Problem	Somewhat Serious Problem	Serious Problem
1. Not having clear and concrete goals for your diabetes care?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Feeling discouraged with your diabetes treatment plan?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Feeling scared when you think about living with diabetes?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Uncomfortable social situations related to your diabetes (e.g., people telling you what to eat)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Feelings of deprivation regarding food and meals?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Feeling depressed when you think of living diabetes?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Not knowing if your mood or feelings are due to your diabetes?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Feeling overwhelmed by your diabetes?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Worrying about low blood sugar reactions?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. Feeling angry when you think about living with diabetes?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11. Feeling constantly concerned about food and eating?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12. Worrying about the future and the possibility of serious complications?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13. Feelings of guilt or anxiety when you get off track with your diabetes management?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
14. Not accepting your diabetes?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
15. Feeling unsatisfied with your diabetes physician?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
16. Feeling that diabetes is taking up too much of your mental & physical energy every day?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
17. Feeling alone with your diabetes?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
18. Feeling that your friends and family are not supportive of your diabetes management efforts?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
19. Coping with complications of diabetes?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
20. Feeling burned out by the constant effort needed to manage diabetes?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Appendix 14

System of care should participant score at clinical levels for anxiety/ depression/
PTSD

Care protocol: 3 month follow-up v1

From the literature (e.g. NICE PTSD guidelines) one would expect clinically significant levels of anxiety and/or depression and/or post traumatic stress disorder symptoms at admission and 1 month follow up. However, if at 3 month follow up participants are self-reporting clinically significant levels of anxiety and/ or depression and/ or post traumatic stress disorder symptoms then the below should be followed.



Appendix 15

NHS Grampian Research and Development Approval

Miss Kirsty Matheson
Trainee Clinical Psychologist
Psycho-Oncology
Roxburghe House
Ashgrove Road
Aberdeen
AB25 3AE

Date 30/08/11
Your Ref [your ref]
Our Ref 2011GD002

Enquiries to
Extension 51121
Direct Line 01224 551121

Dear Miss Matheson

Management Permission for Non-Commercial Research

REC Ref: 11/AL/0339
Project title: Emotional wellbeing following hospital admission for diabetic ketoacidosis

Thank you very much for sending all relevant documentation. I am pleased to confirm that the project is now registered with the NHS Grampian Research & Development Office. The project now has R & D Management Permission to proceed locally. This is based on the documents received from yourself and the relevant Approvals being in place.

All research with an NHS element is subject to the Research Governance Framework for Health and Community Care (2006, 2nd edition), and as Chief or Principal Investigator you should be fully committed to your responsibilities associated with this.

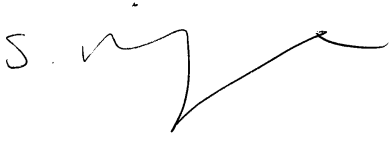
It is particularly important that you inform us when the study terminates.

The R&D Office must be notified immediately and any relevant documents forwarded to us if any of the following occur:

- A change of Principal Investigator, Chief Investigator or any additional research personnel
- Premature project termination
- Any amendments – substantial or non-substantial (particularly a study extension)
- Any change to funding or any additional funding

We hope the project goes well, and if you need any help or advice relating to your R&D Management Permission, please do not hesitate to contact the office.

Yours sincerely

A handwritten signature in black ink, appearing to read 'S. Ridge', with a long, sweeping horizontal stroke extending to the right.

Susan Ridge
Non-Commercial Manager