ISLETS
2020, VOL. 12, NO. 2, 21–31
https://doi.org/10.1080/19382014.2020.1736740

Taylor & Francis
Taylor & Francis Group

RESEARCH PAPER

Characterization of pre-transplant psychosocial burden in an integrated national islet transplant program

Aaron YL Liew [a,b], Elizabeth Holmes-Truscott [c,d], Anneliese JS Flatt [a,b], Denise Bennett[a], Robert Crookston[e], Mirka Pimkova[f], Linda Birtles [g], John Casey[h], Andrew Pernet [i], Ruth C Wood [j], Pratik Choudhary [i], Shareen Forbes [h,k], Martin K Rutter [g,l], Miranda Rosenthal[f], Paul Johnson [e], James AM Shaw [a,b], and Jane Speight [c,d,m]

[a]Institute of Transplantation, Freeman Hospital, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK; [b]Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, UK; [c]School of Psychology, Deakin University, Geelong, Australia; [d]The Australian Centre for Behavioural Research in Diabetes, Diabetes Victoria, Melbourne, Australia; [e]Nuffield Department of Surgery, University of Oxford, John Radcliffe Hospital, Oxford, UK; [f]Institute of Immunity and Transplantation, Royal Free Hospital, London, UK; [g]Manchester Academic Health Science Centre (MAHSC), Manchester Diabetes Centre, Manchester University NHS Foundation Trust, Manchester, UK; [h]Transplant Unit, Royal Infirmary of Edinburgh, Edinburgh, UK; [i]Department of Diabetes, School of Life Course Sciences, King's College London, London, UK; [j]Newcastle Clinical Trials Unit, Newcastle University, Newcastle upon Tyne, UK; [k]BHF Centre for Cardiovascular Sciences, Queen's Medical Research Institute, University of Edinburgh, Edinburgh, UK; [l]Division of Diabetes, Endocrinology and Gastroenterology, School of Medical Sciences, Faculty of Biology, Medicine and Health, Manchester Academic Health Science Centre (MAHSC), University of Manchester, Manchester, UK; [m]AHP Research, Hornchurch, UK

ABSTRACT

The psychological burden experienced by people with diabetes prior to islet transplantation is recognized but has not been studied comprehensively, especially in relation to glycemia. Therefore, we conducted a rigorous pre-operative psychosocial profile of UK islet transplant recipients, and compared groups with higher/lower HbA1 c to test the null hypothesis that pre-transplant hypoglycemia awareness and psychosocial burden would not be related to baseline HbA1 c in this high-risk cohort. Pre-transplant, recipients (n = 44) completed validated hypoglycemia awareness questionnaires and generic/diabetes-specific measures of psychological traits and states. Scores were compared in groups, dichotomized by HbA1 c (≤8% versus >8%). Participants were aged (mean±SD) 53 ± 10 years; 64% were women; with HbA1 c 8.3 ± 1.7%. Median rate of severe hypoglycemia over the preceding 12 months was 13 events/person-year and 90% had impaired awareness of hypoglycemia (Gold/Clarke score ≥4). Participants had elevated fear of hypoglycemia (HFS-II Worry), impaired diabetes-specific quality of life (DQoL) and low generic health status (SF-36; EQ-5D). One quarter reported scores indicating likely anxiety/depression (HAD). Dispositional optimism (LOT-R) and generalized self-efficacy (GSE) were within published 'norms.' Despite negative perceptions of diabetes (including low personal control), participants were confident that islet transplantation would help (BIPQ). Hypoglycemia awareness and psychosocial profile were comparable in lower (n = 24) and higher (n = 20) HbA1 c groups. Islet transplant candidates report sub-optimal generic psychological states (anxiety/depressive symptoms), health status and diabetes-specific psychological states (fear of hypoglycemia, diabetes-specific quality of life). While their generic psychological traits (optimism, self-efficacy) are comparable with the general population, they are highly optimistic about forthcoming transplant. HbA1 c is not a proxy measure of psychosocial burden, which requires the use of validated questionnaires to systematically identify those who may benefit most from psychological assessment and support.

ARTICLE HISTORY
Received 23 May 2019
Revised 20 January 2020
Accepted 24 February 2020

KEYWORDS
Islet transplantation; psychological burden; HbA1c; hypoglycemia awareness; diabetes mellitus

Introduction

Following seminal success with the Edmonton protocol, insulin independence was established as the principal goal for islet transplantation.[1] Edmonton's success has been replicated internationally but sustained insulin independence for more than 3 years cannot be achieved in more than 50% of recipients.[2] In the UK, islet transplantation is established as a fully reimbursed, equitably available intervention, where the goal is resolution of recurrent severe hypoglycemia (i.e., requiring the assistance of another person for

CONTACT James Am Shaw jim.shaw@ncl.ac.uk Translational and Clinical Research Institute, Newcastle University, the Medical School, Framlington Place, Newcastle upon Tyne NE2 4HH, UK; Jane Speight jspeight@acbrd.org.au The Australian Centre for Behavioural Research in Diabetes, Diabetes Victoria, 570 Elizabeth Street, Melbourne, VIC 3000, Australia

recovery)[3] and not insulin independence *per se*. This has been demonstrated alongside improved awareness of hypoglycemia and attainment of optimal HbA1 c (<7%).[3]

Simple assessment of severe hypoglycemia frequency and HbA1 c does not illuminate an individual's experience of living with diabetes. The potential impact of islet transplant on psychological outcomes (for better or worse) has been emphasized.[4–10] Therefore, it is important that pre-transplant psychosocial experience is taken into consideration. Increasingly, patient-reported outcomes (PROs) are considered alongside biomedical outcomes as part of holistic transplant assessment. However, a systematic review showed that PRO assessment in potential islet transplantation recipients has been limited largely to the appraisal of generic health status and/or fear of hypoglycemia.[4] Few studies have conducted a rigorous assessment of psychological burden in this high-risk cohort. The most comprehensive to date found impaired generic mental health status and depressive symptoms, alongside high fear of hypoglycemia and elevated diabetes distress.[11] These factors may predict adaptation to life post-transplant, including the need for lifelong immunosuppression medication.[12] Furthermore, psychological traits, such as dispositional optimism and general self-efficacy, which may also be of consequence, have not been assessed previously in an islet transplantation population.

The inverse relationship between HbA1 c and severe hypoglycemia reported in the landmark Diabetes Control and Complications Trial[13] appears to have driven a belief that sufficiently problematic/frequent severe hypoglycemia to justify islet transplantation occurs only in those with lower HbA1 c. Conversely, it is often considered that suboptimal psychological well-being is only experienced in those with higher HbA1 c. Yet, severe hypoglycemia is associated with considerable psychological burden,[14,15] and recent real-world clinical data demonstrate that severe hypoglycemia occurs in adults with type 1 diabetes regardless of their HbA1 c level.[14,16]

The primary aim of this study was to characterize the pre-transplant self-reported psychological and health burden experienced by recipients in the UK program. We hypothesized that pre-transplant hypoglycemia awareness and psychological burden would not be related to baseline HbA1 c in this high-risk cohort and, therefore, compared those with higher (>8%) and lower (≤8%) HbA1 c at listing for transplantation.[17]

Results

Forty-four consecutive participants consenting to this study completed questionnaires on completion of pre-transplant assessment and activation on the waiting list. All subsequently received one or more islet transplant (70 islet transplants in total). Table 2 summarizes the demographic and clinical characteristics of participants. Sixty-four percent were women. Mean±SD age was 53 ± 10 years, with diabetes duration 34 ± 12 years, BMI 24.9 ± 3.4 kg/m^2 and HbA1 c 8.3 ± 1.7% (67 ± 18 mmol/mol). All had experienced at least two severe hypoglycemia events over the preceding 2 years, fulfilling listing criteria. Within the preceding 12 months, 90% had experienced at least one severe hypoglycemic event, with 55% reporting ≥11 events, and 90% reported impaired awareness of hypoglycemia (Gold and/or Clarke score ≥4).

When demographic and clinical characteristics were compared in the group with higher HbA1 c (>8%: n = 20) versus those with lower HbA1 c (≤8%: n = 24) at listing for transplant, no significant differences were found in severe hypoglycemia rate or other baseline parameters, except a trend toward longer diabetes duration in the lower HbA1 c group (≤8%: 38 ± 12 vs >8%: 30 ± 9 years; p = .028).

Psychosocial outcomes are summarized for the whole cohort and stratified by higher and lower HbA1 c in Table 3. Mean±SD HFS-II Worry score in the overall cohort was 45 ± 15, indicating high fear of hypoglycemia. Mean DQOL subscale scores for Satisfaction, Impact and Diabetes Worry ranged from 47 to 57, indicating impaired diabetes-specific quality of life; while the Social Worry scale had considerable missing data.

Regarding diabetes perceptions (Table 3), study participants reported very high 'Concern' about their diabetes and its impact on their lives ('Consequences'). They perceived that diabetes would 'continue forever' ('Timeline') and reported a negative emotional burden 'making them angry, scared, upset or depressed' ('Emotional representation'). Mid-range scores for

'experiencing symptoms from your diabetes' were reported ('Identity'). While participants reported understanding their diabetes 'clearly' ('Coherence'), they felt little 'Personal control' over their condition. However, participants believed resoundingly that a transplant would 'help their diabetes' ('Transplant control').

Almost half reported clinically relevant (at least mild) depression symptoms (HAD-D ≥ 8: 47%) and/or anxiety symptoms (HAD-A ≥ 8: 49%). SF-36 Summary scores indicated substantial impairment across Mental and Physical components. For the EQ-5D, more than two-thirds reported (some/extreme) problems in Usual Activities and Pain/Discomfort, half reported (some/extreme) problems with Anxiety/Depressive symptoms and Mobility, while one in five had problems with Self-care.

For general psychological traits, the LOT-R and GSES scores indicated that dispositional optimism and generalized self-efficacy were comparable with published norms for the UK general adult population.[18-20]

Impaired awareness of hypoglycemia was comparable in those with higher and lower HbA1 c (Table 3). No significant differences were observed between the two HbA1 c groups for diabetes-specific or generic psychosocial measures, with the exception of a trend toward greater anxiety in those with higher HbA1 c (p = .032). There were no significant differences in self-reported health status for the EQ-5D domains or SF-36 Summary scores.

Discussion

This study provides the most comprehensive psychosocial characterization to date of adults with type 1 diabetes undergoing islet transplantation. It demonstrates that the self-reported psychological and health burden before the procedure is not trivial, with many reporting considerable psychological distress associated with recurrent dangerous hypoglycemia and long disease duration.

Despite problematic hypoglycemia being the major indication for islet transplantation candidacy, fear of hypoglycemia has been assessed in only four previous studies.[6,8,10,21] In the current study, we used the HFS-II, but others have used the original HFS, or used an alternate scoring method for the HFS-II, such that scores are not directly comparable between islet transplantation studies. In the current cohort, mean HFS-II Worry score was twice that of the US validation sample comprising a wide range of individuals with established type 1 diabetes,[22] and comparable with or higher than studies in which participants have reported at least one severe hypoglycemic event within the past 6 months.[14,17] Norms and cut-points to define clinically relevant elevation in fear of hypoglycemia have been established for the HFS-II in adults with type 2[23] but not type 1 diabetes; however, higher scores indicate greater fear and are typically found among those with most frequent and severe hypoglycemia.[22] Listing for islet transplantation in those with recurrent severe hypoglycemia and impaired awareness of hypoglycemia is thus associated with significant pre-transplant fear of hypoglycemia.

Diabetes-specific quality of life was assessed with the DQOL questionnaire in order to enable comparisons with previous islet transplantation studies.[4] Scores suggested lower diabetes-specific quality of life in prospective UK recipients than observed at baseline in other published islet transplant studies,[7,9] and also in a UK study of adults with type 1 diabetes,[24] reflecting the high burden of living with diabetes in the current cohort. These findings are consistent with an in-depth, qualitative study of islet transplant candidates, which demonstrated a high pre-operative psychological burden, predominantly from recurrent, unpredictable severe hypoglycemia, with considerable negative impact on quality of life.[5]

At the point of joining the islet transplantation waiting list, questionnaire screening indicative of 'caseness' for anxiety and depression was detected in one quarter and one-fifth of the participants, respectively. The HAD scale can offer only an *indicator* of symptom severity, which requires confirmation with a clinical diagnostic interview. While these rates appear concerning, they are similar to those reported in epidemiological studies and meta-analyses of the general type 1 diabetes population.[25-27] For example, these pre-transplant rates are highly comparable with those observed in a large cohort (n = 639) – 24% had 'caseness' for anxiety and 21% for depression – prior to attending a UK structured type 1 diabetes education program.[28] Importantly, it has been noted elsewhere

that questionnaire-based scores of generic anxiety/depression show moderate-to-strong correlations with diabetes-related distress.[23]

The Brief Illness Perceptions Questionnaire has not previously been completed by prospective islet transplant recipients. This confirmed how severely life is affected by diabetes in this select, high-risk cohort, leading to a high level of concern and considerable emotional impact. Participants felt little control over their diabetes, and perceived that islet transplantation would be extremely helpful. Despite being on the islet transplant list they had a clear perception that their diabetes would continue forever. It was notable, however, in the preceding qualitative study, that UK islet transplant recipients hoped for at least 'a break from diabetes.'[5] They reported realistic expectations, having being counseled that long-term insulin independence was not a goal, but many retained 'hidden hopes of being among the minority to remain insulin free.'

While participants reported a high level of confidence that the transplant would help their diabetes, their general dispositional optimism was comparable to the general UK adult population[18,19] and somewhat lower than that of Dutch adults with type 1 diabetes.[29] Generalized self-efficacy levels among the current islet transplantation recipients were also comparable with the general UK adult population[20] and with Dutch adults with type 1 diabetes.[29] Many studies have highlighted the positive health benefits of an optimistic outlook, though these have tended to focus on outcomes of cardiovascular disease and cancer. A previous qualitative study of islet transplant candidates demonstrated that they were willing to accept the potential risks associated with transplantation and ongoing immunosuppression.[5] Psychological traits, such as dispositional optimism and general self-efficacy, were also shown to be important for how participants dealt with the uncertainty of 'life on the list' for a transplant.[5] This is the first islet transplantation cohort in which these psychological traits have been assessed quantitatively. Given that islet transplantation involves accepting, adapting and coping with the procedure and its consequences, it will be of interest to note in future studies, whether high expectations for transplantation (which may or may not be realized) and/or more generally optimistic beliefs impact upon biomedical outcomes and quality of life following islet transplantation.

Previous studies of conventional non-transplant intervention for severe hypoglycemia[17] have dichotomized participants into groups with HbA1 c ≤ 8% (to capture those with a strong primary motivation to avoid all high glucose excursions) and >8% (characterized by higher glucose variability) and we agreed on *a priori* to dichotomize the current pre-islet transplant cohort using this HbA1 c value. HbA1 c was >8% in just under half of those studied. All fulfilled the listing criteria of recurrent severe hypoglycemia with comparable impaired awareness of hypoglycemia and fear of hypoglycemia scores to those with lower HbA1 c. All diabetes and generic psychosocial scores in this highly selected cohort were very similar in higher and lower HbA1 c groups, with the exception of a trend toward greater anxiety in those with higher HbA1 c, consistent with studies in a wider spectrum of adults with type 1 diabetes.[30] This underlines the negative psychological impact and burden of severe hypoglycemia and impaired awareness of hypoglycemia, irrespective of baseline HbA1 c.

This study has several clinical implications. Clinicians need to be aware that individuals listed for islet transplantation are characterized by the considerable psychological burden and impact of their problematic hypoglycemia on well-being and quality of life; and that this is irrespective of whether baseline HbA1 c is in a higher or lower range. Furthermore, individuals considering islet transplantation exhibit high levels of confidence that the procedure can alleviate this burden, despite having only an averagely optimistic disposition in comparison to the wider population. As noted previously, these high expectations need to be recognized by transplant teams, and strategies considered for how best to support the individual in coping with disappointments at any stage.[5] Since its inception, the UK national program has included provision for psychological assessment of suitability for islet transplantation, mandated as part of the multidisciplinary team decision for inclusion on the waiting list.[31] The Diabetes UK patient guide 'Islet Cell Transplant: What You Need to Know' indicates that a meeting with a clinical psychologist will be arranged to

determine whether 'extra psychological support during or after the procedure' may be needed.[32] In addition to ruling out major psychological/psychiatric co-morbidity, a particular focus is on assessing the individual's level of understanding of the potential risks as well as benefits of islet transplantation, and determining whether they have realistic expectations. It is not clear whether expert psychological evaluation is embedded within other programs internationally.[33] Informed by the current study, we recommend formal-structured psychological assessment of all potential islet transplant recipients, to include evaluation of fear of hypoglycemia, diabetes-specific quality of life, anxiety/depressive symptoms and perceptions/expectations of the procedure. This will enable identification and follow-up of individualized psychological needs pre- and post-transplantation, facilitating provision of evidence-based support and intervention as required. This should augment adoption of the evidence-informed clinical pathways, which have been proposed in recent years to guide the therapeutic strategies offered to those with problematic hypoglycemia, including those under assessment for or awaiting islet transplant.[34] The absence of statistically significant differences in psychosocial questionnaire outcomes between those with higher versus lower pre-transplant HbA1 c further underlines the importance of holistic assessment of all potential islet recipients using validated tools and approaches, in parallel with baseline biomedical evaluation.

The current study has several strengths. It is a multi-center, multi-disciplinary study, recruiting a cohort of patients within the first national health service funded program of islet transplantation as an established clinical intervention for prevention of severe hypoglycemia and achievement of HbA1 c < 7%. It is the largest and most comprehensive study to date of the psychosocial characterization of adults undergoing islet transplantation. Furthermore, this study used validated generic and diabetes-specific psychological measures to characterize both psychological traits and states. This study also has several limitations, including a relatively small sample compared with non-islet transplant studies. There is no control group, as it was designed as a cohort study. We have not reported data on diabetes-related complications beyond confirmation of satisfactory renal function through serum creatinine. Despite few missing data overall, the completion rate for DQOL Social Worry subscale was very low, in keeping with the previously observed low face validity of this section of the questionnaire for an adult cohort.[35]

In summary, we have conducted detailed baseline profiling of a relatively large islet transplant cohort. Overall, these adults with long-standing type 1 diabetes exhibit considerable diabetes-specific psychological burden (i.e., lower diabetes-specific quality of life, greater fear of hypoglycemia and equivalent anxiety/depressive symptoms) compared with the wider adult population with type 1 diabetes in the UK. Their psychological traits (e.g., optimistic beliefs) are comparable to the general population, though they exhibit extremely high levels of confidence in the ability of islet transplantation to help with their diabetes. Furthermore, this study highlights that HbA1 c is not a proxy measure for underlying psychological burden. Comprehensive diabetes-specific psychosocial evaluation needs to be integral to the multidisciplinary assessment of whether islet transplantation will be suitable for an individual with type 1 diabetes; and ongoing psychosocial support will be needed throughout the transplant process.

Patients and methods

The integrated UK Islet Transplant Consortium (UKITC) program comprises seven National Health Service commissioned centers: Bristol, Edinburgh, King's College London, Royal Free London, Manchester, Newcastle and Oxford. Following ethical approval from the NRES Committee North East – Tyne and Wear South (REC reference 07/Q0904/11) and informed written consent, a prospective cohort of consecutive individuals were recruited fulfilling all consensus inclusion criteria for islet transplantation without exclusion criteria (Table 1). In parallel with pre-listing biomedical assessment, all were invited to complete psychological measures at the point of joining the transplant waiting list between

Table 1. Inclusion and exclusion criteria for the UK islet transplant program

Inclusion criteria	Exclusion criteria
• Age: ≥18 years • Diagnosis: C-peptide-negative diabetes • History: recurrent severe hypoglycemia (at least two events over the preceding 24 months requiring assistance from another person to administer carbohydrate, glucagon or other resuscitative actions[36]) despite optimized conventional management	• Insulin resistance (insulin requirement >0.7 U/kg) • Any contraindication to immunosuppression, including impaired renal function with isotopic GFR<60 mL/min/1.73 m^2 or albumin excretion rate >300 mg/24 h (unless previous renal transplant)

Table 2. Demographic and clinical characteristics of islet transplant recipients (n = 44)

Gender, woman	28 (64%)
Age, years	53.1 ± 10.0
Diabetes duration, years	34.4 ± 11.5
BMI, kg/m^2	24.9 ± 3.4
HbA1 c, %	8.3 ± 1.7
mmol/mol	67 ± 18
Insulin dose, Units/kg/day	0.52 ± 0.19
Creatinine, µmol/l	89.8 ± 36.2
Severe hypoglycemia, events per person-year	13.0 (3.5–51.0) [0–51.0]
• 0	4 (10.0%)
• 1	2 (5.0%)
• 2–4	5 (12.5%)
• 5–10	7 (17.5%)
• 11–20	5 (12.5%)
• 21–50	5 (12.5%)
• >50	12 (20.0%)

Data are n (%) or, depending on distribution, mean±SD or median (IQR) [range].

Missing datapoints were apparent for creatinine (n = 42) and severe hypoglycemia (n = 40).

April 2008 and March 2011. All subsequently received one or more islet transplant(s).

Demographic and clinical data included HbA1 c and number of self-reported severe hypoglycemia events over the preceding 12 months.[36] A comprehensive set of psychological characteristics and outcomes were assessed, as described below.

Hypoglycemia awareness

The Gold Score[37] is a single question ("do you know when your hypos are commencing?") rated on a 7-point Likert scale, from 1 = 'always aware' to 7 = 'never aware.' The eight-item Clarke Questionnaire[38] assesses occurrence of moderate and severe hypoglycemia, and experience of hypoglycemic symptoms. Responses to each question are categorized as either 'aware' or 'reduced awareness.' For both the Gold score and the Clarke questionnaire, a score of ≥4 indicates impaired awareness of hypoglycemia.

Fear of hypoglycemia

The Hypoglycemia Fear Survey-II (HFS-II)[39] includes 33 statements, rated in terms of how often each has been a concern in the last 6 months, from 0 = 'never' to 4 = 'almost always.' Eighteen item scores are summed to create a 'worry' score (range: 0–72), where higher scores indicate greater worry about hypoglycemia and its negative consequences. Fifteen item scores are summed to form a 'behaviour' score (range: 0–60), where higher scores indicate increased behavior to avoid hypoglycemia and its negative consequences.

Diabetes-specific quality of life

The Diabetes Quality Of Life questionnaire (DQOL)[40] includes 46 items across four subscales: 'life satisfaction' (15 items), 'diabetes impact' (20 items), 'worries about diabetes' (4 items), and 'social/vocational concerns' (7 items). All items are scored on a 5-point Likert scale (from 1 ('very satisfied,' 'no impact, or 'no worry') to 5 ('very dissatisfied,' 'always impacted,' or 'always worried')). Subscale scores are calculated by taking the sum of items (reversing scores as needed) and converting this raw total to a score out of 100. Higher scores indicate better diabetes-specific quality of life.

Perceptions of diabetes

The Brief Illness Perceptions Questionnaire (BIPQ)[41] includes eight items, each one assessing a different dimension (e.g., perceived control, emotional impact). Each item is rated on an 11-point scale (from 0 to 10), where higher scores indicate greater endorsement of that dimension. According to convention, the questionnaire was made condition-specific for the current study, by replacing 'illness' with 'diabetes,' and replacing 'treatment' with 'transplant.' For item 3 ('How much control, do you have over your diabetes?') and item 7 ('How well do you feel you understand

Table 3. Pre-transplant psychosocial characteristics, for whole sample and stratified by HbA1c

			HbA1c				
Diabetes-specific psychosocial states	n	Whole sample	n	≤8% (n = 24)	n	>8% (n = 20)	p-Value
Hypoglycemia awareness							
• Gold score (1–7)	30	6.0 (6.0–7.0) [1–7]	17	7.0 (6.0–7.0)	13	6.0 (6.0–7.0)	.234 [b]
• Clarke questionnaire (0–7)	30	6.0 (5.0–7.0) [1–7]	16	5.5 (5.0–7.0)	14	6.0 (6.0–7.0)	.644 [b]
Fear of hypoglycemia							
• HFS-II Worry (0–72)	40	45.2 ± 15.3	21	45.7 ± 15.4	19	44.8 ± 15.4	.867 [a]
• HFS-II Behavior (0–60)	39	34.4 ± 13.3	22	31.0 ± 14.4	17	38.9 ± 10.6	.066 [a]
Diabetes-specific quality of life (0–100)							.206 [a]
• DQoL Satisfaction	43	56.8 ± 16.8	23	59.8 ± 17.4	20	53.3 ± 15.8	.359 [a]
• DQoL Impact	42	51.7 ± 13.3	23	53.5 ± 13.3	19	49.6 ± 13.4	.069 [a]
• DQoL Social Worry	8	75.6 ± 15.7	5	83.2 ± 13.2	3	62.9 ± 11.3	.921 [a]
• DQoL Diabetes Worry	44	47.3 ± 22.0	24	47.7 ± 18.1	20	47.0 ± 26.5	
Perceptions of diabetes (0–10)							
• BIPQ Consequences	43	9 (8–10) [4–10]	23	9.0 (8.0–10)	20	8.5 (7.5–10.0)	.543 [b]
• BIPQ Timeline	43	10 (10–10) [0–10]	24	10.0 (10–10)	19	10 (10–10)	.732 [b]
• BIPQ Personal control	43	3 (1–6) [0–10]	24	4.0 (0.25–8.0)	19	3.0 (1.0–6.0)	.413 [a]
• BIPQ Transplant control	42	10 (8–10) [7–10]	23	10 (8.0–10.0)	19	10 (8.0–10)	.852 [b]
• BIPQ Identity	41	8 (4–9) [0–10]	23	8.0 (5.0–10)	18	6.5 (1.0–9.0)	.158 [b]
• BIPQ Illness concern	42	10 (9–10) [3–10]	24	10.0 (8.5–10)	18	10 (9.0–10)	1.000 [b]
• BIPQ Coherence	42	10 (8–10) [0–10]	23	10 (9.0–10)	19	9.0 (8–10)	.298 [b]
• BIPQ Emotional representation	44	8 (5.5–10) [0–10]	24	8.0 (5.0–9.5)	20	8.5 (7.5–10)	.290 [b]
Generic psychosocial states and traits							
Anxiety symptoms: HAD-A (0–21)	43	7.9 ± 4.9	23	6.4 ± 4.6	20	9.6 ± 4.8	.032 [a]
• HAD-A ≥ 8	21	21 (48.8)	9	9 (39.1)	12	12 (60.0)	.221 [a]
• HAD-A ≥ 11 ('caseness')	11	11 (26.6)	2	2 (8.7)	9	9 (45.0)	
Depressive symptoms: HAD-D (0–21)	43	6.9 ± 4.4	23	6.1 ± 4.4	20	7.8 ± 4.4	
• HAD-D ≥ 8	20	20 (46.5)	11	11 (47.8)	9	9 (45.0)	
• HAD-D ≥ 11 ('caseness')	9	9 (20.9)	5	5 (21.7)	4	4 (20.0)	
Dispositional optimism: LOT-R (0–24)	44	11.8 ± 4.4	24	12.2 ± 5.0	20	11.3 ± 3.7	.500 [a]
Generalized self-sfficacy: GSES (10–40)	42	29.2 ± 4.6	22	30.4 ± 4.8	20	27.9 ± 3.9	.080 [a]
Generic health status							
SF-36v2 Summary scores (0–100)							
• Mental component	41	40.0 ± 13.7	22	43.2 ± 12.9	19	36.3 ± 14.1	.110 [a]
• Physical component	41	43.0 ± 8.2	22	43.8 ± 7.7	19	42.0 ± 8.8	.486 [a]
EQ-5D-3 L (% with some/extreme problems)							
• Mobility	41	22 (53.7%)	23	11 (47.8%)	18	11 (61.1%)	.397 [c]
• Self-care	42	9 (21.4%)	23	3 (13.0%)	19	6 (31.6%)	.257 [d]
• Usual activities	42	29 (69.0%)	23	17 (73.9%)	19	12 (63.2%)	.453 [c]
• Pain/discomfort	42	29 (69.1%)	23	15 (65.2%)	19	14 (73.7%)	.555 [c]
• Anxiety/depression	41	24 (55.8%)	22	12 (54.5%)	19	12 (63.2%)	.577 [c]

Data are n (%) or, depending on distribution, mean±SD or median (IQR) [range]. Differences analyzed using [a]Student's t-test, [b]Mann-Whitney U test, [c]Chi-square test or [d]Fisher's exact test.

For each measure the potential range is shown in the left-hand column next to the name of the measure or subscale. Higher scores Gold and Clarke Score indicate likely impaired awareness of hypoglycemia. Higher scores on the HFS-II indicate increased worry about, and behavior to avoid hypoglycemia and its negative consequences. Higher scores on the DQOL indicate better diabetes-specific quality of life, while higher scores on the SF-36 indicate better general physical or mental health status. Higher scores on the BIPQ indicate greater endorsement of the named dimension (perception of diabetes). Higher HAD scores indicate greater anxiety or depression symptomatology. Higher scores on the LOT-R indicate a greater disposition toward optimism. Higher GSES scores indicates greater confidence in one's capacity for coping.

your diabetes?'), higher scores indicate more positive perceptions of diabetes. Item 4 is the only treatment-specific question ('How much do you think your transplant can help your diabetes?'), with higher scores referring to a more positive perception. For all other items, higher scores indicate more negative perception of diabetes impact.

Anxiety and depressive symptoms

The Hospital Anxiety and Depression (HAD) scale[42] includes two 7-item subscales: 'anxiety' and 'depression.' Respondents rate items using a 4-point scale (from 0 to 3). Item scores are summed to form subscale scores (from 0 to 21), with higher scores indicating greater anxiety or

depression symptomatology. A score of ≥8 indicates at least mild anxiety or depression symptoms (borderline 'caseness'), while a score of ≥11, indicating moderate-to-severe symptoms, is regarded as 'caseness.'[42]

Optimistic beliefs

Outcome expectancies were measured with the Life Orientation Test – Revised [LOT-R],[43] which includes 10 statements rated on a 5-point Likert scale, where 0 = 'strongly agree' and 4 = 'strongly disagree.' The three pessimism item scores are reversed and added to the three optimism item scores, while four 'filler' items are ignored. Total scores range from 0 to 24, with higher scores indicating a greater disposition toward optimism. Participants also completed the Generalized Self-Efficacy Scale (GSES)[44] includes 10 statements rated on a 4-point scale, where 1 = 'not at all true' and 4 = 'exactly true.' Item scores are summed to create a total score ranging from 10 to 40, with higher scores indicating greater confidence in one's capacity for coping.

Generic health status

The SF-36v2[45] is a 36-item questionnaire that yields two summary scores: Physical Component Score and Mental Component Score (each ranging from 0 to 100). Participants also completed the EQ-5D-3 L[46] tariff, which comprises five items or dimensions of general health rated using three response options ('no problems,' 'some problems,' 'extreme problems'). For the current study, we report the proportion of participants experiencing 'some/extreme problems' for each dimension. For both SF-36 and EQ-5D, higher scores indicate better general health status and lower scores indicate more health limitations.

Statistical analyses were conducted using STATA statistical package version 14.1 (StataCorp, Texas, USA). For all psychological measures, missing data were handled with expectation-maximization imputation for up to 10% missing data, unless the questionnaire guidelines stated otherwise. For the DQOL, subscale scores were not computed if respondents had more missing data than deemed acceptable in the scoring guideline.[40] Categorical data were expressed as n (%). Continuous data were expressed as mean ± standard deviation (SD) or median (interquartile range) [range] as appropriate to the data distribution. Demographic, clinical and psychological outcomes were compared in participants with higher (>8%), and lower (≤8%) HbA1c.[17] Comparisons were conducted using Student's t-test for parametric data and Mann-Whitney U test for non-parametric data. Categorical variables were compared using the Chi-square test, or Fisher's exact when the expected values in any of the cells of a contingency table are below 5, or below 10 when there is only one degree of freedom. Given the number of statistical tests, and the exploratory nature of the analysis, significance was set at $p < .01$.

Abbreviations

BIPQ	Brief Illness Perceptions Questionnaire
DQOL	Diabetes Quality Of Life (questionnaire)
EQ-5D-3L	EuroQoL Five Dimensions (questionnaire)
HAD	Hospital Anxiety and Depression (scale)
HbA1c	Hemoglobin A1c
HFS-II	Hypoglycemia Fear Survey – Version II (questionnaire)
LOT-R	Life Orientation Test – Revised (questionnaire)
GSES	Generalized Self-Efficacy Scale (questionnaire)
SF-36	Short-Form 36 items (questionnaire)
UK	United Kingdom
UKITC	UK Islet Transplant Consortium

Disclosure of Potential Conflict of Interest

A. Liew: *Advisory Panel*: AstraZeneca, Novo Nordisk, Sanofi, Lilly, Amgen, MSD, Janssen; *Speaker fee/Travel support*: AstraZeneca, Boehringer Ingelheim, Sanofi, Lilly, MSD, Novo Nordisk

E. Holmes-Truscott: *Advisory Panel*: Astra Zeneca; *Research Support*: Abbott Diabetes Care, Astra Zeneca, Sanofi ANZ; *Speaker fee*: Novo Nordisk

M.K. Rutter: *Consultant*: Roche Pharmaceuticals, Roche Diabetes Care and Novo Nordisk Inc; Stock/Shareholder: GSK; *Speaker fees and travel support*: Novo Nordisk

P. Choudhary: *Speaker fees and travel support*: Novo Nordisk, Lilly, Sanofi, Novartis, Medtronic, Roche, Insulet, Abbott and Dexcom.

P. Johnson: *Advisory Panel*: Dompe Pharmaceutical, Defymed (UK and Sweden)

J.A.M. Shaw: *Travel support*: Novo Nordisk; *Advisory Panel*: Novo Nordisk, Sanofi; *Speaker fee*: Medtronic, Novo Nordisk.

J. Speight: *Advisory Panels*: Medtronic, Sanofi ANZ; *Consultant*: Abbott Diabetes Care; *Research Support*: Abbott Diabetes Care, Astra Zeneca, Medtronic, Roche Diabetes Care, Sanofi ANZ; *Other relationships*: Astra Zeneca, Novo Nordisk, Sanofi ANZ.

All other authors declare no conflicts of interest.

Acknowledgments

We thank all the islet transplant recipients for participating in this study. In addition, we thank the UKITC Centres: Prof Stephanie Amiel, Guo Cai Huang, Steve Hughes, Lora Irvine, Wendy Littlejohn, Parthi Srinivasan; Newcastle/NHSBT: Catherine Brennand, Michael Cole, Sue Madden, Jonathan Prichard, Deborah Stocken, Sharon Weatherburn; AHP Research: Dr Alison Woodcock and Matthew Reaney for their early contributions during the planning phase, and David Wilson for data entry of psychological measures.

Funding

This work was undertaken within the centrally commissioned National Health Service UK islet transplant programme, coordinated through the UK Islet Transplant Consortium and funded by Diabetes UK (BDA: 06/0003362). The research was supported by the National Institute for Health Research Newcastle Biomedical Research Centre;

Authorship

JS and JAMS determined the psychological measures to be included in the UKITC dataset, in liaison with the UK Islet Transplant Consortium. JS, JAMS, AL and EHT developed the plan for this study. EHT prepared the psychological dataset, AF prepared the biomedical dataset and AL and EHT conducted statistical analyses. JS and AL prepared the first draft, with input from EHT and JAMS. All other authors reviewed the draft and provided critical input. All authors approved the final version.

ORCID

Aaron YL Liew http://orcid.org/0000-0002-6274-0253
Elizabeth Holmes-Truscott http://orcid.org/0000-0001-9139-4663
Anneliese JS Flatt http://orcid.org/0000-0003-4315-5136
Linda Birtles http://orcid.org/0000-0002-6078-8456
Andrew Pernet http://orcid.org/0000-0002-1950-4925
Ruth C Wood http://orcid.org/0000-0002-8296-1774
Pratik Choudhary http://orcid.org/0000-0001-7635-4735
Shareen Forbes http://orcid.org/0000-0002-9127-0641
Martin K Rutter http://orcid.org/0000-0001-6380-539X
Paul Johnson http://orcid.org/0000-0003-3142-137X
James AM Shaw http://orcid.org/0000-0002-2893-3211
Jane Speight http://orcid.org/0000-0002-1204-6896

References

1. Shapiro AM, Lakey JR, Ryan EA, Korbutt GS, Toth E, Warnock GL, Kneteman NM, Rajotte RV. Islet transplantation in seven patients with type 1 diabetes mellitus using a glucocorticoid-free immunosuppressive regimen. N Engl J Med. 2000;343(4):230–238. doi:10.1056/NEJM200007273430401.
2. Shapiro AM, Ricordi C, Hering BJ, Auchincloss H, Lindblad R, Robertson RP, Secchi A, Brendel MD, Berney T, Brennan DC, et al. International trial of the Edmonton protocol for islet transplantation. N Engl J Med. 2006;355(13):1318–1330. doi:10.1056/NEJMoa061267.
3. Brooks AM, Walker N, Aldibbiat A, Hughes S, Jones G, de Havilland J, Choudhary P, Huang GC, Parrott N, McGowan NWA, et al. Attainment of metabolic goals in the integrated UK islet transplant program with locally isolated and transported preparations. Am J Transplant. 2013;13(12):3236–3243. doi:10.1111/ajt.12469.
4. Speight J, Reaney MD, Woodcock AJ, Smith RM, Shaw JA. Patient-reported outcomes following islet cell or pancreas transplantation (alone or after kidney) in Type 1 diabetes: a systematic review. Diabet Med. 2010;27(7):812–822. doi:10.1111/dme.2010.27.issue-7.
5. Speight J, Woodcock AJ, Reaney MD, Amiel SA, Johnson P, Parrott N, Rutter MK, Senior P, Shaw JAM. Well, I wouldn't be any worse off, would I, than I am now? A qualitative study of decision-making, hopes, and realities of adults with type 1 diabetes undergoing islet cell transplantation. Transplant Direct. 2016;2(5):e72. doi:10.1097/TXD.0000000000000581.
6. Foster ED, Bridges ND, Feurer ID, Eggerman TL, Hunsicker LG, Alejandro R. Improved health-related quality of life in a phase 3 islet transplantation trial in type 1 diabetes complicated by severe hypoglycemia. Diabetes Care. 2018;41(5):1001–1008. doi:10.2337/dc17-1779.
7. Tharavanij T, Betancourt A, Messinger S, Cure P, Leitao CB, Baidal DA, Froud T, Ricordi C, Alejandro R. Improved long-term health-related quality of life after islet transplantation. Transplantation. 2008;86(9):1161–1167. doi:10.1097/TP.0b013e31818a7f45.
8. Toso C, Shapiro AM, Bowker S, Dinyari P, Paty B, Ryan EA, Senior P, Johnson JA. Quality of life after islet transplant: impact of the number of islet infusions and metabolic outcome. Transplantation. 2007;84(5):664–666. doi:10.1097/01.tp.0000280550.01028.89.
9. Poggioli R, Faradji RN, Ponte G, Betancourt A, Messinger S, Baidal DA, Froud T, Ricordi C, Alejandro R. Quality of life after islet transplantation. Am J Transplant. 2006;6(2):371–378. doi:10.1111/ajt.2006.6.issue-2.
10. Haggstrom E, Rehnman M, Gunningberg L. Quality of life and social life situation in islet transplanted patients: time for a change in outcome measures? Int J Organ Transplant Med. 2011;2:117–125.
11. Radosevich DM, Jevne R, Bellin M, Kandaswamy R, Sutherland DE, Hering BJ. Comprehensive health assessment and five-yr follow-up of allogeneic islet transplant recipients. Clin Transplant. 2013;27(6):E715–724. doi:10.1111/ctr.12265.

12. Dobbels F, Vanhaecke J, Dupont L, Nevens F, Verleden G, Pirenne J, De Geest S. Pretransplant predictors of posttransplant adherence and clinical outcome: an evidence base for pretransplant psychosocial screening. Transplantation. 2009;87(10):1497–1504. doi:10.1097/TP.0b013e3181a440ae.
13. Chase HP, Lockspeiser T, Peery B, Shepherd M, MacKenzie T, Anderson J, Garg SK. The impact of the diabetes control and complications trial and humalog insulin on glycohemoglobin levels and severe hypoglycemia in type 1 diabetes. Diabetes Care. 2001;24 (3):430–434. doi:10.2337/diacare.24.3.430.
14. Hendrieckx C, Halliday JA, Bowden JP, Colman PG, Cohen N, Jenkins A, Speight J. Severe hypoglycaemia and its association with psychological well-being in Australian adults with type 1 diabetes attending specialist tertiary clinics. Diabetes Res Clin Pract. 2014;103 (3):430–436. doi:10.1016/j.diabres.2013.12.005.
15. Wild D, von Maltzahn R, Brohan E, Christensen T, Clauson P, Gonder-Frederick L. A critical review of the literature on fear of hypoglycemia in diabetes: implications for diabetes management and patient education. Patient Educ Couns. 2007;68(1):10–15. doi:10.1016/j.pec.2007.05.003.
16. Miller KM, Foster NC, Beck RW, Bergenstal RM, DuBose SN, DiMeglio LA, Maahs DM, Tamborlane WV. Current state of type 1 diabetes treatment in the U.S.: updated data from the T1D Exchange clinic registry. Diabetes Care. 2015;38(6):971–978. doi:10.2337/dc15-0078.
17. Little SA, Leelarathna L, Walkinshaw E, Tan HK, Chapple O, Lubina-Solomon A, Chadwick TJ, Barendse S, Stocken DD, Brennand C, et al. Recovery of hypoglycemia awareness in long-standing type 1 diabetes: a multicenter 2 × 2 factorial randomized controlled trial comparing insulin pump with multiple daily injections and continuous with conventional glucose self-monitoring (HypoCOMPaSS). Diabetes Care. 2014;37(8):2114–2122. doi:10.2337/dc14-0030.
18. Walsh D, McCartney G, McCullough S, van der Pol M, Buchanan D, Jones R. Always looking on the bright side of life? Exploring optimism and health in three UK post-industrial urban settings. J Public Health (Oxf). 2015;37(3):389–397. doi:10.1093/pubmed/fdv077.
19. Glaesmer H, Rief W, Martin A, Rief, W., Martin, A., Mewes, R., Brähler, E., Zenger, M., and Hinz, A. Psychometric properties and population-based norms of the Life Orientation Test Revised (LOT-R). Br J Health Psychol. 2012;17(2):432–445. doi:10.1111/j.2044-8287.2011.02046.x.
20. Schwarzer R. General perceived self-efficacy in 14 cultures. http://userpagefu-berlinde/~gesund/publicat/ehps_cd/health/world14htm.
21. Barshes NR, Vanatta JM, Mote A, Lee TC, Schock AP, Balkrishnan R, Brunicardi FC, Goss JA. Health-related quality of life after pancreatic islet transplantation: a longitudinal study. Transplantation. 2005;79 (12):1727–1730. doi:10.1097/01.TP.0000160816.21799.F5.
22. Gonder-Frederick LA, Schmidt KM, Vajda KA, Greear ML, Singh H, Shepard JA, Cox DJ. Psychometric properties of the hypoglycemia fear survey-ii for adults with type 1 diabetes. Diabetes Care. 2011;34(4):801–806. doi:10.2337/dc10-1343.
23. Hajos TR, Polonsky WH, Pouwer F, Gonder-Frederick L, Snoek FJ. Toward defining a cutoff score for elevated fear of hypoglycemia on the hypoglycemia fear survey worry subscale in patients with type 2 diabetes. Diabetes Care. 2014;37(1):102–108. doi:10.2337/dc13-0971.
24. Taylor MD, Frier BM, Gold AE, Deary IJ. Edinburgh prospective diabetes s. psychosocial factors and diabetes-related outcomes following diagnosis of type 1 diabetes in adults: the edinburgh prospective diabetes study. Diabet Med. 2003;20(2):135–146. doi:10.1046/j.1464-5491.2003.00887.x.
25. Gilsanz P, Schnaider Beeri M, Karter AJ, Quesenberry CP Jr., Adams AS, Whitmer RA. Depression in type 1 diabetes and risk of dementia. Aging Ment Health. 2019;23(7):880–886.
26. Smith KJ, Beland M, Clyde M, Gariépy G, Pagé V, Badawi G, Rabasa-Lhoret R, Schmitz N. Association of diabetes with anxiety: a systematic review and meta-analysis. J Psychosom Res. 2013;74(2):89–99. doi:10.1016/j.jpsychores.2012.11.013.
27. Gendelman N, Snell-Bergeon JK, McFann K, Kinney G, Paul Wadwa R, Bishop F, Rewers M, Maahs DM. Prevalence and correlates of depression in individuals with and without type 1 diabetes. Diabetes Care. 2009;32(4):575–579. doi:10.2337/dc08-1835.
28. Hopkins D, Lawrence I, Mansell P, Thompson G, Amiel S, Campbell M, Heller S. Improved biomedical and psychological outcomes 1 year after structured education in flexible insulin therapy for people with type 1 diabetes: the U.K. DAFNE experience. Diabetes Care. 2012;35(8):1638–1642. doi:10.2337/dc11-1579.
29. Fournier M, De Ridder D, Bensing J. Optimism and adaptation to chronic disease: the role of optimism in relation to self-care options of type 1 diabetes mellitus, rheumatoid arthritis and multiple sclerosis. Br J Health Psychol. 2002;7(Part 4):409–432. doi:10.1348/135910702320645390.
30. van Bastelaar KM, Pouwer F, Geelhoed-Duijvestijn PH, Pouwer, F, Tack, C.J., Bazelmans, E., Beekman, A.T., Heine, R.J., and Snoek, F.J. Diabetes-specific emotional distress mediates the association between depressive symptoms and glycaemic control in type 1 and type 2 diabetes. Diabet Med. 2010;27(7):798–803. doi:10.1111/j.1464-5491.2010.03025.x.
31. Flatt AJS, Bennett D, Counter C, Brown AL, White SA, Shaw JAM. beta-Cell and renal transplantation options for diabetes. Diabet Med. 2019. doi:10.1111/dme.14177.
32. Rutter MK, Amiel S, Birtles L, Casey J, Choudhary P, Duncan K, Forbes S, Johnson P, Jones G, Parrott N, et al.

On behalf of the UK islet transplant consortium. islet cell transplant. What you need to know; 2017. https://diabetes-resources-productions3-eu-west-1amazonawscom/diabetes-storage/migration/pdf/Islet%2520cell%2520transplant%2520PDF%2520Mar%25202017pdf.
33. Clinical Guidelines For Pancreatic Islet Transplantation. 2014. http://wwwtransplantbcca/Documents/Health%20Professionals/Clinical%20guidelines/Clinical%20Guidelines%20for%20Pancreatic%20Islet%20Transplantation_01Sept2014_0pdf.
34. Choudhary P, Rickels MR, Senior PA, Vantyghem M-C, Maffi P, Kay TW, Keymeulen B, Inagaki N, Saudek F, Lehmann R, et al. Evidence-informed clinical practice recommendations for treatment of type 1 diabetes complicated by problematic hypoglycemia. Diabetes Care. 2015;38(6):1016–1029. doi:10.2337/dc15-0090.
35. Speight J, Reaney MD, Barnard KD. Not all roads lead to Rome-a review of quality of life measurement in adults with diabetes. Diabet Med. 2009;26(4):315–327. doi:10.1111/dme.2009.26.issue-4.
36. Seaquist ER, Anderson J, Childs B, Cryer P, Dagogo-Jack S, Fish L, Heller SR, Rodriguez H, Rosenzweig J, Vigersky R, et al. Hypoglycemia and diabetes: a report of a workgroup of the American diabetes association and the endocrine society. Diabetes Care. 2013;36(5):1384–1395. doi:10.2337/dc12-2480.
37. Gold AE, MacLeod KM, Frier BM. Frequency of severe hypoglycemia in patients with type I diabetes with impaired awareness of hypoglycemia. Diabetes Care. 1994;17(7):697–703. doi:10.2337/diacare.17.7.697.
38. Clarke WL, Cox DJ, Gonder-Frederick LA, Julian D, Schlundt D, Polonsky W. Reduced awareness of hypoglycemia in adults with IDDM. A prospective study of hypoglycemic frequency and associated symptoms. Diabetes Care. 1995;18(4):517–522. doi:10.2337/diacare.18.4.517.
39. Cox DJ, Irvine A, Gonder-Frederick L, Nowacek G, Butterfield J. Fear of hypoglycemia: quantification, validation, and utilization. Diabetes Care. 1987;10(5):617–621. doi:10.2337/diacare.10.5.617.
40. Reliability and validity of a diabetes quality-of-life measure for the diabetes control and complications trial (DCCT). The DCCT Research Group. Diabetes Care. 1988;11(9):725–732. doi:10.2337/diacare.11.9.725.
41. Broadbent E, Petrie KJ, Main J, Weinman J. The brief illness perception questionnaire. J Psychosom Res. 2006;60(6):631–637. doi:10.1016/j.jpsychores.2005.10.020.
42. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67(6):361–370. doi:10.1111/acp.1983.67.issue-6.
43. Scheier MF, Carver CS, Bridges MW. Distinguishing optimism from neuroticism (and trait anxiety, self-mastery, and self-esteem): a reevaluation of the Life Orientation Test. J Pers Soc Psychol. 1994;67(6):1063–1078. doi:10.1037/0022-3514.67.6.1063.
44. Schwarzer RJM. Generalized self-efficacy scale. In: Weinman. J, Wright. S, Johnson. M editors. Measures in health psychology: a users portfolio Causal and control beliefs (pp. 35–37). Windsor, UK: NFER-NELSON, 1995.
45. Ware Jr JE, K, M.B, J.b, Turner-BowkerDM, Gandek B, Maruish ME. User's manual for the SF-36v2 health survey. Rhode Island (RI): Quality Metric Lincoln; 2008.
46. Konerding U, Elkhuizen SG, Faubel R, Forte P, Malmström T, Pavi E, Janssen MB. The validity of the EQ-5D-3L items: an investigation with type 2 diabetes patients from six European countries. Health Qual Life Outcomes. 2014;12:181. doi:10.1186/s12955-014-0181-5.