

Continuing Professional Development



60 Second Summary

Diabetic ketoacidosis (DKA) continues to be a common cause of admission in type 1 diabetes and is the leading cause of mortality in young people with type 1 diabetes.

Historically, patients who presented with rDKA were often described as having 'brittle diabetes', and the difficulties of these patients often confounded the best efforts of clinicians and researchers.

When a person is diagnosed with type 1 diabetes they immediately have to acquire a host of new self-management skills that include monitoring of blood glucose, adjustment of diet and exercise to avoid hyper- or hypoglycaemia and management of what is usually referred to as "sick day rules".

The principles of management of DKA that are included in Guidelines such as those of the Joint British Diabetes Societies emphasise (1) establishing a definite diagnosis of DKA, (2) early administration of adequate fluid replacement, (3) commencement of a fixed dose insulin infusion according to the patient's weight and (4) close monitoring of blood glucose, ketones and electrolytes with adjustment of the DKA protocol based on the patient's response.

If rDKA it cannot be explained, i.e. causes such as new diagnosis of diabetes, concomitant infection, insulin pump failure etc., it may be due to psychosocial factors, and rDKA which is unexplained should always trigger a psychosocial assessment.

As well as elevated levels of diabetes distress, rDKA may be related to other psychosocial factors. It is important to consider any psychosocial factors that might be contributing to these dangerous presentations including diabetes distress and mental disorders such as eating disorders or depression.

AUTHORS:

Tara Garman, MB BCH BAO, Senior House Officer, Galway University Hospitals

Tara graduated from NUI Galway recently and is currently working as a Senior House Officer with the Endocrinology Department in Galway University Hospital. She has a strong interest in Diabetes & Endocrinology and hopes to pursue a career in this specialty.

Eimear C Morrissey, BA, MSc, PhD

Postdoctoral Researcher, Health Behaviour Change Research Group, School of Psychology & School of Medicine, National University of Ireland, Galway

Eimear is a health psychologist and postdoctoral researcher at the School of Medicine and School of Psychology at NUI Galway. She is currently working as Programme Manager of D1 Now – a Health Research Board funded project which aims to improve outcomes for young adults living with type 1 diabetes. Her research interests include self-management of chronic disease, behavior change science and public and patient involvement in research.

Anne M Doherty, MB BCH BAO, MRCPsych, MMedSc, MD

Associate Professor of Psychiatry, University College Dublin
Consultant Liaison Psychiatrist, Mater Misericordiae University Hospital Dublin.

Prior to her 2020 appointment to UCD and the Mater Hospital, Anne was consultant in liaison psychiatry at Galway University Hospitals. From 2012 - 2016, she was Consultant Liaison Psychiatrist at King's College Hospital, London, leading the 3 Dimensions of Care for Diabetes service, an award-winning (BMJ Team of the Year Award 2014) multi-disciplinary team for people with poorly controlled diabetes. Her research interests include adjustment disorders, suicidality, and the interface between psychiatry and diabetes.

Seán F Dinneen, MD, MSc, FRCPI, National Lead for the Diabetes Clinical Programme, HSE

Consultant Endocrinologist, Galway University Hospitals
Professor of Diabetes Medicine, National University of Ireland, Galway

Sean is currently Consultant Endocrinologist at Galway University Hospital and holds a Personal Professorship in Diabetic Medicine at NUI Galway. He served as Head of the School of Medicine at NUI Galway from 2013 to 2016. In June 2016 he was appointed National Lead for the Diabetes Clinical Programme of the HSE. His professional interests include developing and evaluating programmes of self-management, education and support for people living with diabetes, developing optimal modules of community-based diabetes care and understanding the diabetic foot.

1. REFLECT - Before reading this module, consider the following: Will this clinical area be relevant to my practice?

2. IDENTIFY - If the answer is no, I may still be interested in the area but the article may not contribute towards my continuing professional development (CPD). If the answer is yes, I should identify any knowledge gaps in the clinical area.

3. PLAN - If I have identified a knowledge gap - will this article satisfy those needs - or will more reading be required?

4. EVALUATE - Did this article meet my learning needs - and how has my practise changed as a result? Have I identified further learning needs?

5. WHAT NEXT - At this time you may like to record your learning for future

use or assessment. Follow the 4 previous steps, log and record your findings.

Published by HPN.
Copies can be downloaded from www.irishpharmacytraining.ie

Disclaimer: All material published is copyright, no part of this can be used in any other publication without permission of the publishers and author.

Recurrent diabetic ketoacidosis: A guide to comprehensive mind-body management

Recurrent diabetic ketoacidosis

Diabetic ketoacidosis (DKA) continues to be a common cause of admission in type 1 diabetes and is the leading cause of mortality in young people with type 1 diabetes.¹ It is a complex disordered metabolic state characterised by hyperglycaemia, acidosis, and ketonaemia.² Complete or near complete absence of insulin leads to hyperglycaemia through the failure of insulin-mediated cellular uptake of glucose and fatty acid breakdown becomes unregulated, resulting in ketone production and acidosis. If untreated or unrecognised, coma and death occur within 3–4 days.¹ The guidelines of the Joint British Diabetes Societies for Inpatient Care define recurrent DKA (rDKA) as 2 or more unexplained episodes of DKA.³ Historically, patients who presented with rDKA were often described as having 'brittle

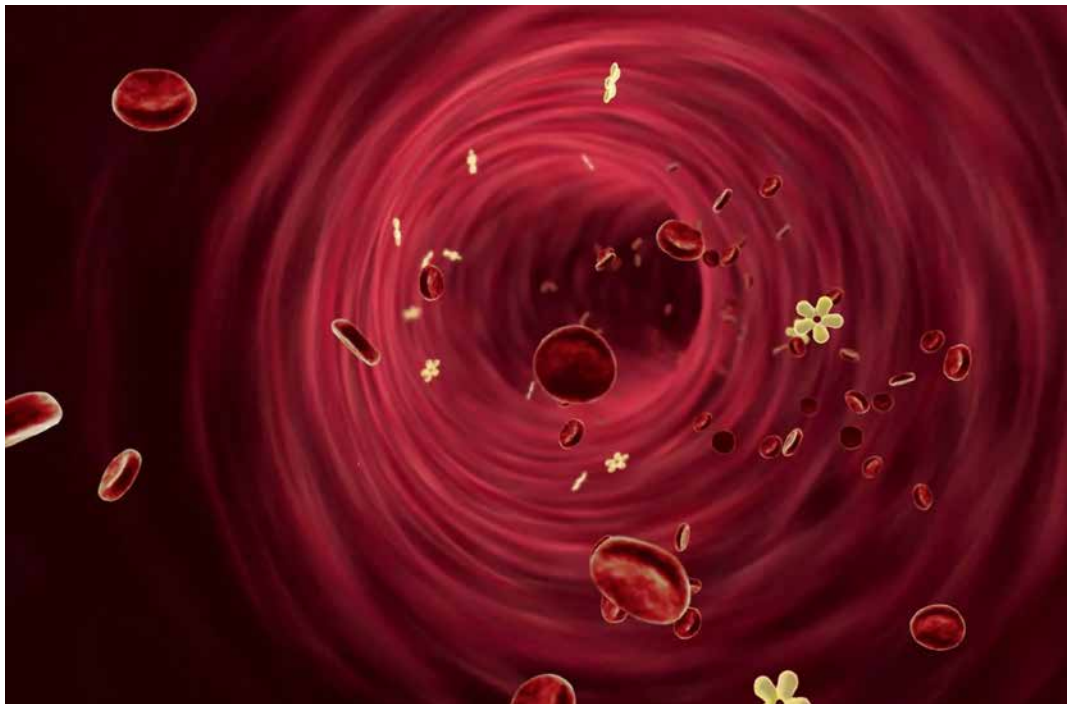
diabetes', and the difficulties of these patients often confounded the best efforts of clinicians and researchers.¹

Case study

A 22 year old female with type 1 diabetes since age 6 has struggled to achieve optimal control of her diabetes and would very likely (if a proper definition existed) fulfil the criteria for "brittle diabetes". The patient transitioned from Paediatric to Young Adult Diabetes services at 18 years of age. Her time in Paediatrics was marked by multiple admissions to hospital for investigation of recurrent vomiting and abdominal pain of uncertain aetiology. Many of these hospitalisations were precipitated by episodes of DKA. These medical problems occurred on a background of anxiety, depression, concerns about weight and many psychosocial issues relating to difficult home circumstances.

During the four years that she has been registered with the Young Adult Diabetes service she has continued to have frequent admissions to hospital with DKA but has also demonstrated a pattern of recurrent (and difficult to explain) hypoglycaemia including episodes of severe hypoglycaemia requiring input from paramedics or others to assist with treatment. For a period of 2 years the patient did not attend any of her scheduled outpatient appointments. She admits to ongoing difficulty with anxiety and depression, but has been unable to engage with Psychology Services beyond an initial visit. Her caregivers suspect that there may be a psychological component to her recurrent vomiting; perhaps an attempt to manage her weight.

Her psychosocial difficulties have continued from adolescence into young adulthood; as well as ongoing family strife she has had



difficulty maintaining education/employment and admits to occasional use of illicit drugs. Of concern she has early signs of microvascular complications in her retina and peripheral nerves within 15 years of diagnosis of childhood onset diabetes.

Commentary

The term brittle diabetes was coined by Robert Tattersall, a British Physician, who stated in 1977: "For the purposes of the practising physician, the [term] brittle diabetes is most simply defined as [occurring in a] patient whose life is constantly being disrupted by episodes of hypo- or hyperglycaemia whatever their cause...". Tattersall did not differentiate between psychological or biological causes of brittle diabetes. Although the biomedical orientation of many Endocrinologists would favour finding a "biological cause" that might lead to a "cure", the reality is that in many patients (including the patient illustrated in our Case Study) a biopsychosocial approach may be more appropriate. Whether the underlying cause is biological or psychological, the sad reality is that a similar fate (of premature morbidity and mortality) often awaits these patients highlighting an urgent need for more investigation into this challenging clinical syndrome. In this article we will briefly review the management of diabetic ketoacidosis and then explore the relatively

uncharted waters of recurrent DKA representing a signal for underlying diabetes distress.

Prevention and management of DKA

When a person is diagnosed with type 1 diabetes they immediately have to acquire a host of new self-management skills that include monitoring of blood glucose, adjustment of diet and exercise to avoid hyper- or hypoglycaemia and management of what is usually referred to as "sick day rules". The latter refer to a set of principles or actions aimed at avoiding hospitalisation due to the development of diabetic ketoacidosis when a person is acutely unwell. These principles include monitoring blood (glucose and ketones) more frequently, taking an appropriate amount of quick-acting insulin, maintaining a reasonable level of hydration, converting food into more easily digestible forms and never stopping the basal insulin. The commonest mistake made by patients during sick days is to think "I'm not eating; therefore I don't need insulin". More often than not this error of omission leads to worsening of the metabolic crisis and precipitates hospitalisation.

The principles of management of DKA that are included in Guidelines such as those of the Joint British Diabetes Societies 2 emphasise (1) establishing a

definite diagnosis of DKA, (2) early administration of adequate fluid replacement, (3) commencement of a fixed dose insulin infusion according to the patient's weight and (4) close monitoring of blood glucose, ketones and electrolytes with adjustment of the DKA protocol based on the patient's response. If insulin omission is the commonest mistake made by patients when managing sick days then premature discontinuation of intravenous insulin before the ketoacidosis has fully resolved is the commonest mistake made by hospital doctors in managing DKA. Although blood glucose will likely reduce quickly it can take much longer to fully clear the ketosis and acidosis requiring conversion from a saline-based fluid replacement regimen to a dextrose (or dextrose/saline) based regimen. The latter permits the intravenous insulin infusion to be continued until the DKA has fully resolved.

Recurrent DKA and diabetes distress

If rDKA it cannot be explained, i.e. causes such as new diagnosis of diabetes, concomitant infection, insulin pump failure etc., it may be due to psychosocial factors, and rDKA which is unexplained should always trigger a psychosocial assessment.³ One possible causal factor for rDKA is elevated levels of diabetes distress.⁴ Diabetes distress (hereafter referred to as distress) can be conceptualised as the negative emotional burden of

living with diabetes.⁵ While much research on the psychological aspects of living with diabetes has focused on depression, it is increasingly clear that distress is a distinct emotional construct rooted in the worries, fears and concerns of individuals contending with a chronic condition.⁶ It is not a psychiatric disorder, such as those discussed below, although if left untreated it can result in more generalised negative affect.⁷ Traditionally seen as a complication of diabetes, Gonzalez, Fisher and Polonsky suggest it is more suitably viewed as the emotional aspect of living with this challenging chronic condition.⁸ The same authors postulate that distress exists on a single continuous dimension that is characterised by content and severity.⁶ The content can be made up of distress in relation to diabetes and self-management (e.g. fear of hypos) but also distress related to other life stressors (e.g. family, finances) and distress from other causes (e.g. life history, genetics). It is important not to lose sight of the non-diabetes related causes of distress because these can often impact on self-management and diabetes related difficulties. The severity of distress can fluctuate throughout the lifespan⁶ and it is estimated that about one third of adults with diabetes are living with elevated levels of distress at any one time.⁹

Assessment

If an individual is presenting with rDKA it may be advisable to screen for diabetes distress. There have been several measurement tools developed to screen for distress. Two that are widely used to assess distress are the Problem Areas in Diabetes scale (PAID) and the Diabetes Distress Scale (DDS).^{5,10} The PAID is a 20 item scale of diabetes specific emotional distress that measures a wide range of feelings related to living with diabetes and its management, including guilt, anger, depressed mood, worry and fear. It is scored from 0-100 with higher scores indicating greater distress. A score above 40 is considered the threshold for elevated distress.¹¹ The DDS is a 17 item scale that captures 4 dimensions of distress: emotional burden, regimen distress, interpersonal distress and physician distress.⁵ It yields a total distress score as well as the four subscale scores. A mean item score of 3 or higher on either the total score or any of the subscale scores is considered

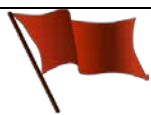


Table 1: 'Red flags' for formal psychiatric evaluation in diabetes (adapted from Garrett et al) (1)

Suicidal ideation or behaviours
Evidence of depressed mood
Recurrent admissions (i.e. for recurrent DKA or severe hypoglycaemia)
Difficulties at transition from paediatric to adult services
Persistent suboptimal glycaemic control
Low BMI (may indicate eating disorder)
Reluctance to commence insulin therapy in type 2 diabetes (consider needle phobia)

the cut-off for distress worthy of clinical attention.¹⁰ Both the PAID and the DDS are available in short form.

Management

In practice, people who have elevated levels of distress can be supported by diabetes health services which

(1) Promote positive communication which invites discussion about emotional aspects of living with diabetes and

(2) Provide psychoeducation and practical supports for self-management of diabetes.

Positive communication involves use of empathetic listening, reflective comments and considerate enquiry. The language used around diabetes is important; it should be person-centred, inclusive and collaborative such as that proposed by the UK National Health Service 'Language Matters' report.¹² If the individual is experiencing severe distress a referral to psychological services may be required. Secondly, the particular aspect of diabetes that the individual is finding distressing may be possible to address through provision of practical supports within the clinic, for example, through referral to structured education courses and provision of access to technologies that can improve self-management such as continuous glucose monitors or insulin pumps.¹³ This approach of positive communication and provision of practical tools for self-management allows relationships to build between the young person and staff within the diabetes clinic and supports engagement with self-management and diabetes care.¹⁴

Recurrent DKA and mental disorders

As well as elevated levels of diabetes distress, rDKA may be related to other psychosocial factors. Insulin omission is the leading cause of DKA, and where this is the case, it is important to explore why.¹⁵ A French population-based study found that 7% of patients with type 1 diabetes and a history of DKA were hospitalised during the nine year follow up period compared to 2.5% of individuals with type 1 diabetes and no history of DKA. The rate increased to 16.2% among those patients with DKA and co-morbid history of mental illness. The rates were highest in the first 12 months following the admission for DKA, which indicates that the immediate aftermath of a DKA admission may be a time of greater need.¹⁶

Bryden et al reported that having a psychiatric diagnosis predicted DKA, and indeed DKA predicted the development of a mental disorder at 10 years.¹⁷ Garrett et al, in a review of the literature around 'brittle' diabetes note that there is a gap in the evidence for the medium/long term management of same.¹ Among adolescents, Goldston et al found that suicidal thoughts were strongly associated with poor engagement with diabetes self-management.¹⁸ Roberts et al reported that people with type 1 diabetes had a significantly increased rate of suicide: 11 times that of the general population.¹⁹ Subsequent studies have confirmed an elevated rate of suicide among people with diabetes, although not to the same magnitude.

Self-harm can be active with obvious suicide attempts (which

may involve overdose of insulin or another hypoglycaemic agent) or more occult, manifesting as repeated admissions for DKA, severe hypoglycaemia or other medical complications related to diabetes. This may be viewed as ambivalence towards living with diabetes or an indirect suicidal wish.

Depression

Diabetes can present a particular challenge in the management of suicidal ideations and behaviours given that insulin, the essential treatment for type one diabetes (and used by many individuals with type 2 diabetes) is potentially lethal in overdose. Poor adherence to the medical regimen could be considered another form of self-destructive behavior and one that must be taken seriously. In particular, adolescents who have a lifetime history of suicidal ideation were found to be have difficulties with adherence their medical regimen.²⁰ A systematic review reported that patients with both type 1 and type 2 diabetes have an increased incidence of depression: approximately twice that of the general population (9% compared with 5%) and a still larger proportion, up to one quarter, have subclinical depressive symptoms.²¹

People with diabetes and depression are more likely to have poorer outcomes, with poorer glycaemic control, greater rates of diabetic complications and higher mortality rates. This suggests that depression may be regarded as a modifiable risk factor for the morbidity and mortality in diabetes due to its role as a barrier to optimal self-management.²² These poor outcomes may be related to difficulties with interest, motivation and energy all of which are associated with depression

and pose difficulties for optimal diabetes self-management. In particular, the lifestyle modification that is an important part of the management of diabetes can be difficult to accomplish in patients with co-morbid depression.

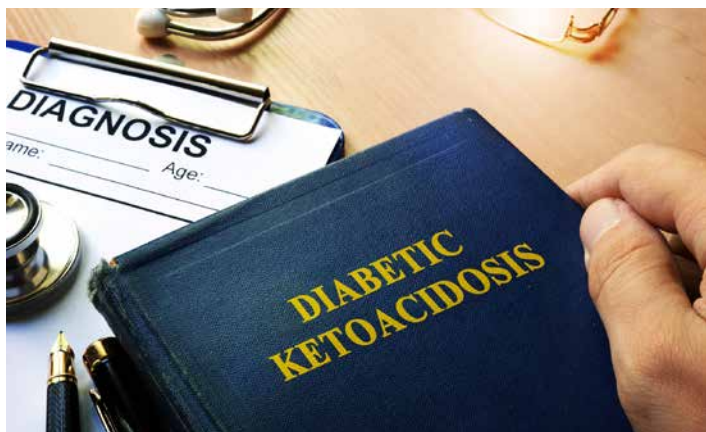
Eating disorders

Eating disorders are common in diabetes, and where present are associated with poorer outcomes. Nielsen's 10 year follow up study found that the standardised mortality rate for people with type one diabetes was 2.5%, but 6.5% for people with anorexia nervosa and 34.8% in those with both conditions.²³ This is due to the fact that where eating disorders and diabetes are co-morbid, patients frequently purge by insulin omission. Patients with these co-morbidities will have poorer glycaemic control reflected in high HbA1c values, and may present with rDKA. With a high index of suspicion for disordered eating, assessment of the patient with rDKA should always include a discussion about weight and insulin omission, and a referral onwards to liaison psychiatry, eating disorder psychiatry or the local community mental health team as appropriate. It is important to have a higher index of suspicion in patients with persistently elevated HbA1c, rDKA and with ketonuria.

Assessment

All patients presenting to hospital with self-harm, suicidal behaviours or suicidal ideation should receive a full mental health assessment before discharge. Patients with diabetes who are admitted with self-harm, or a suicidal attempt should routinely be asked about suicidal ideation.²⁴

The guidelines of the Joint British Diabetes Societies – Royal College of Psychiatry (JBDS- RCPsych) recommend that all patients who present with rDKA should have a formal mental health assessment preferably by a liaison psychiatrist with expertise in diabetes. The JBDS- RCPsych guidelines acknowledge that patients with psychological and social problems may struggle to access the usual pathways and access to diabetes care. Using DKA as a red flag for a psychiatric assessment will improve detection of these problems, by identifying patients who require referral for formal psychiatric assessment and treatment, as in Table 1.³



Management

Although there are clear guidelines for the management of diabetes emergencies, there are few studies or guidelines that inform the management of patients with diabetes and mental illness where psychological considerations have an important role in the aetiology of primarily physical presentations. Here, the inpatient admission should be regarded as a ‘window of opportunity’ to identify and initiate integrating psychological care to support self-management.¹

Conclusion

DKA is a complex disordered metabolic state characterised by hyperglycaemia, acidosis, and ketonaemia. Despite advances in the medical management of type 1 diabetes it remains a common cause of admission in type 1 diabetes, and is the leading cause of mortality in young people with type 1 diabetes. It is important to consider any psychosocial factors that might be contributing to these dangerous presentations including diabetes distress and mental disorders such as eating disorders or depression. These conditions are potentially treatable and should be considered where recurrent DKA is unexplained.

References

- Garrett CJ, Choudhary P, Amiel SA, Fonagy P, Ismail K. Recurrent diabetic ketoacidosis and a brief history of brittle diabetes research: contemporary and past evidence in diabetic ketoacidosis research including mortality, mental health and prevention. *Diabet Med.* 2019;36(11):1329-1335. doi:10.1111/dme.14109
- Joint British Diabetes Societies. The Management of Diabetic Ketoacidosis in Adults. Published online 2013. <https://www.diabetes.org.uk/resources-s3/2017-09/Management-of-DKA-241013.pdf>
- Joint British Diabetes Societies, Royal College of Psychiatrists. Management of diabetes in adults and children with psychiatric disorders in inpatient settings. Published online 2017. Accessed November 12, 2020. <https://www.diabetes.org.uk/professionals/resources/shared-practice/inpatient-and-hospital-care/joint-british-diabetes-society-for-inpatient-care/management-of-diabetes-in-adults-and-children-with-psychiatric-disorders-in-inpatient-settings>
- Hessler D, Fisher L, Polonsky W, et al. Diabetes distress is linked with worsening diabetes management over time in adults with type 1 diabetes. *Diabet Med.* 2017;34(9):1228-1234.
- Polonsky WH, Anderson BJ, Lohrer PA, et al. Assessment of diabetes-related distress. *Diabetes Care.* 1995;18(6):754-760.
- Fisher L, Gonzalez JS, Polonsky WH. The confusing tale of depression and distress in patients with diabetes: a call for greater clarity and precision. *Diabet Med.* 2014;31(7):764-772.
- Skinner TC, Joensen L, Parkin T. Twenty-five years of diabetes distress research. *Diabet Med.* 2019;n/a(n/a). doi:10.1111/dme.14157
- Gonzalez JS, Fisher L, Polonsky WH. Depression in diabetes: have we been missing something important? *Diabetes Care.* 2011;34(1):236-239.
- Sturt J, Dennick K, Hessler D, Hunter BM, Oliver J, Fisher L. Effective interventions for reducing diabetes distress: systematic review and meta-analysis. *Int Diabetes Nurs.* 2015;12(2):40-55.
- Polonsky WH, Fisher L, Earles J, et al. Assessing psychosocial distress in diabetes: development of the diabetes distress scale. *Diabetes Care.* 2005;28(3):626-631.
- Welch GW, Jacobson AM, Polonsky WH. The Problem Areas in Diabetes Scale: An evaluation of its clinical utility. *Diabetes Care.* 1997;20(5):760-766. doi:10.2337/diacare.20.5.760
- National Health Service England. Language Matters: Language and Diabetes. Published online 2018. <https://www.england.nhs.uk/wp-content/uploads/2018/06/language-matters.pdf>
- Balfe M, Doyle F, Smith D, et al. What’s distressing about having type 1 diabetes? A qualitative study of young adults’ perspectives. *BMC Endocr Disord.* 2013;13(1):25.
- Morrissey EC, Casey B, Dinneen SF, Lowry M, Byrne M. Diabetes distress in adolescents and young adults living with type 1 diabetes. *Can J Diabetes.* Published online 2020.
- Umpierrez G, Korytkowski M. Diabetic emergencies – ketoacidosis, hyperglycaemic hyperosmolar state and hypoglycaemia. *Nat Rev Endocrinol.* 2016;12(4):222.
- Petit J-M, Goueslard K, Chauvet-Gelinier J-C, et al. Association between hospital admission for ketoacidosis and subsequent suicide attempt in young adults with type 1 diabetes. *Diabetologia.* 2020;63(9):1745-1752.
- Bryden KS, Dunger DB, Mayou RA, Peveler RC, Neil HAW. Poor prognosis of young adults with type 1 diabetes: a longitudinal study. *Diabetes Care.* 2003;26(4):1052-1057.
- Goldston DB, Kelley AE, Reboussin DM, et al. Suicidal ideation and behavior and noncompliance with the medical regimen among diabetic adolescents. *J Am Acad Child Adolesc Psychiatry.* 1997;36(11):1528-1536.
- Roberts SE, Goldacre MJ, Neil HAW. Mortality in young people admitted to hospital for diabetes: database study. *BMJ.* 2004;328(7442):741-742.
- Jones S, Howard L, Thornicroft G. “Diagnostic overshadowing”: worse physical health care for people with mental illness. Published online 2008.
- Anderson RJ, Freedland KE, Clouse RE, Lustman PJ. The prevalence of comorbid depression in adults with diabetes: a meta-analysis. *Diabetes Care.* 2001;24(6):1069-1078.
- Ismail K, Winkley K, Stahl D, Chalder T, Edmonds M. A cohort study of people with diabetes and their first foot ulcer: the role of depression on mortality. *Diabetes Care.* 2007;30(6):1473-1479.
- Nielsen S, Emborg C, Mølbak A-G. Mortality in concurrent type 1 diabetes and anorexia nervosa. *Diabetes Care.* 2002;25(2):309-312.
- National Collaborating Centre for Mental Health. Depression: the treatment and management of depression in adults (NICE Clinical Guideline 90). *Lond Natl Inst Health Clin Excell.* Published online 2009.



Tara Garman, MB BCh BAO



Eimear C Morrissey, BA, MSc, PhD



Anne M Doherty, MB BCh BAO, MRCPsych, MMedSc, MD



Seán F Dinneen, MD, MSc, FRCPI