

Psychological aspects of diabetes care: Effecting behavioral change in patients

Boon-How Chew, Sazlina Shariff-Ghazali, Aaron Fernandez

Boon-How Chew, Sazlina Shariff-Ghazali, Department of Family Medicine, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia
 Aaron Fernandez, Department of Psychiatry, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia

Author contributions: Chew BH, Shariff-Ghazali S and Fernandez A contributed to this paper.

Correspondence to: Boon-How Chew, MD, Department of Family Medicine, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia. chewboonhow@gmail.com

Telephone: +60-3-89472520 Fax: +60-3-89472328

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Abstract

Patients with diabetes mellitus (DM) need psychological support throughout their life span from the time of diagnosis. The psychological make-up of the patients with DM play a central role in self-management behaviors. Without patient's adherence to the effective therapies, there would be persistent sub-optimal control of diseases, increase diabetes-related complications, causing deterioration in quality of life, resulting in increased healthcare utilization and burden on healthcare systems. However, provision of psychosocial support is generally inadequate due to its challenging nature of needs and demands on the healthcare systems. This review article examines patient's psychological aspects in general, elaborates in particular about emotion effects on health, and emotion in relation to other psychological domains such as cognition, self-regulation, self-efficacy and behavior. Some descriptions are also provided on willpower, resilience, illness perception and proactive coping in relating execution of new behaviors, coping with future-oriented thinking and influences of illness perception on health-related behaviors. These psychological aspects are further discussed in relation

to DM and interventions for patients with DM. Equipped with the understanding of the pertinent nature of psychology in patients with DM; and knowing the links between the psychological disorders, inflammation and cardiovascular outcomes would hopefully encourages healthcare professionals in giving due attention to the psychological needs of patients with DM.

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Key words: Psychology; Psychosocial aspects; Emotions; Cognition; Distress; Depression; Psychological resilience; Self-care; Coping behaviors; Quality of life; Diabetes mellitus

Core tip: Positive psychological health may sustain long-term coping efforts and protect patients from the negative consequences of prolonged emotional disorders, illness perception and thus facilitating diabetes self-management behaviors and better physical health. Having patients acquire valued personal beliefs and achievable standards of performance could strengthen self-regulation and self-efficacy leading to more positive experience and healthy behaviors. Furthermore, improved personal resources such as resilience would lead to better functioning of cognition and stronger will power, quality of life and disease control in patients with diabetes mellitus.

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INTRODUCTION

It is widely known that patients with diabetes mellitus

(DM) are at high risk of decreased psychological well-being^[1-6] which is already present in about half of the patients at the time of diagnosis^[7]. This is due to strained coping with changed life routine (such as relationships, work-related and financial issues)^[6] right from the time of diagnosis of DM^[7]. An international survey, the Diabetes Attitudes, Wishes and Needs second study (DAWN2), included over 16000 individuals (comprising patients, family members and healthcare providers) in 17 countries across four continents, reported that the proportion of the people with DM who were likely to have depression and diabetes-related distress (DRD) was 13.8% and 44.6%, respectively, with overall poor quality of life at 12.2%^[8].

DM had a negative impact on many aspects of life, ranging from 20.5% on relationship with family or friends to 62.2% on physical health. About 40% (18.6%-64.9%) of these patients reported their medication interfered with their ability to live a normal life^[8]. Furthermore, these patients often use negative coping strategies and more frequently perceive that diabetes would negatively affect their future^[4,7]. Untreated psychosocial disorders in DM, may lead to more physical symptoms^[9], cardiovascular complications^[10] and depression^[11,12]. Depression may lead to cognitive decline and further aggravate the vicious cycles of self-care ability^[13]. Many previous studies have largely been on the relationship between depression and diabetes^[14,15], with the focus on major depressive disorder. However, sub-syndromal depressive and milder emotional conditions, such as dysthymia, anxiety, stress and distress^[16], are far more prevalent than major depressive disorder especially at the primary or community care levels^[17,18]. Furthermore, these emotional disorders are linked to increased disability, risk of health decline, healthcare use and premature mortality^[17,19,20]. Despite the widespread prevalence of psychological problems and their negative consequences, the availability of person-centered chronic illness care and psychological support was low for patients with DM. Only 48.8% had received psychological treatment or educational activities to help manage their diabetes^[8]. This review discusses patients' psychological aspects in general with a focus on emotion effects on health, and emotion in relation to other psychological domains such as cognition, resilience, willpower, self-efficacy and behavior. Furthermore, this review reports recent findings on the links between psychological disorders, inflammation and cardiovascular outcomes in patients with DM.

Equipped with the understanding of the pertinent nature and impacts of psychology in patients with DM, it is hoped that this review would encourage healthcare professionals in giving due attention to the psychological needs of patients with DM.

RESEARCH

We conducted searches of multiple databases [MEDLINE® *via* PubMed®, Embase®, Cochrane Register of

Controlled trials, CINAHL (EBSCO), PsycINFO] using terms for emotion, cognition, human behavior, psychosocial and psychological aspects in diabetes care, including but not limited to MeSH terms for emotional disorders, depression, anxiety, stress, distress, diabetes mellitus and psychological interventions. We obtained additional articles from systematic reviews; reference lists of pertinent studies and editorials. We compiled a narrative synthesis of findings, highlighting underlying theories, mechanisms and interactions of the different and essential psychological aspects of patients that might influence self-care behaviors and clinical outcomes.

HEALTH EFFECTS OF EMOTIONS?

Under-expression or over-regulation of emotions with all the other dysfunctional control of emotions could be both the causes for and results of inappropriate emotional responses, personality or even psychiatric disorders^[21,22]. These have been inevitably shown to be associated with physical health^[11,23,24] and DM^[25].

Conversely but in parallel to previous observations, Pressman and Cohen proposed links between positive affect or emotions and health^[26]. They suggest that emotion has a direct effect on both behavior and physiology. More specifically, they hypothesized that positive emotions, such as happiness, excitement and contentment result in better health behaviors and improved adherence to treatment regimens. Direct physiological effects include autonomic nervous system activation, hypothalamic-pituitary-adrenal axis activation (decreased cortisol), and on immune functioning through the primary (bone marrow and thymus) and secondary (spleen and lymph nodes) lymphoid tissues^[27,28]. Indeed, some evidence exists for a moderating effect of emotions on natural killer cell activity^[29]. In a 20-year follow-up study^[30], baseline feeling of vigorous at work among the healthy employees had lower risk of mortality (HR = 0.74, 95%CI: 0.58-0.95) and incidence of diabetes (HR = 0.83, 95%CI: 0.68-0.98) after adjusting for the total cholesterol, glucose, body mass index, smoking, alcohol intake, physical activity, depressive and anxiety symptoms. Healthy behavior such as physical activity causes endorphin excretion leading to a sense of elation^[31], which further reinforces the behavior through operant conditioning. It appears then that as if there is a "spiraling up" of positive effects from physical and psychological being within a person in contrast to the opposite "vicious cycle" of negative emotions.

The pathways between negative and positive emotions and health outcomes interact through behavioral and/or biological mediators, both of which have relevance for DM, an illness characterized by underlying inflammatory changes^[32,33]. Negative emotions can intensify a variety of health threats. Stress, anxiety and depression are related to impaired immune, pro-inflammatory cytokines and inflammation responses that have been linked to a spectrum of conditions associated with aging, including cardiovascular diseases, osteoporosis, arthritis,

Alzheimer's disease, frailty and functional decline, DM, certain cancers and periodontal diseases^[24,34]. Additionally, negative emotions could contribute to prolonged infections and delayed wound healing, conditions that further enhance pro-inflammatory cytokine production^[24]. Accordingly, distress-related immune dysregulation may be the underlying mechanism of a larger and diverse set of health risks associated with negative emotions. Thus, the relationship between emotional disorders and inflammatory responses is likely to be synergistic and bi-directional- the vicious cycle effect^[34].

WHAT IS EMOTION?

An overarching aspect of theoretical perspectives represented in the past three decades of research is that emotion and cognition, though often perceived as having separate functional features and influences^[35,36], are indeed highly interactive and integrated in the brain^[37-39]. This notion is consistent with the high degree of connectivity within the brain's neural structures and systems. Therefore, emotion is hypothesized to have substantial and measurable effects on cognition and action (behavior) when the stimulus or situation is personally or socially significant to the person involved^[37,40]. The key principle of differential emotions theory states that emotions play central role in consciousness and awareness, having dynamic neurobiological and neuropsychological activities that lead to continuous emotions-cognitions interaction in influencing adaptive thoughts and actions as manifested in decision making and behavior^[40].

Physiologically, emotion constitutes brain responses and body expressions^[41]. Although there is no consensus on a general definition of the term "emotion"^[42], many experts do agree that emotions have a limited set of components and characteristics. In addition, emotions have an infrastructure that includes neural systems dedicated in parts to emotion processes and recruit response systems when emotions motivate cognition and action. The autonomic nervous system modulates the intensity of the emotions but does not change its quality or valence. Feeling is a component of emotion that is always experienced or felt, though not necessarily labeled or articulated or present in access consciousness (a level of consciousness that has reportable content). It is considered to be a phase (not a consequence) of neurobiological activity that is sensed by the organism^[40] and was reported to be present and expressed even in children without a cerebral cortex^[43]. Current evidence suggests that in goal-oriented behaviors, the feeling component of emotions contribute its effect to the evolution of consciousness, cognition and action processes resulting in the behaviors^[40].

There is a consensus that emotions exist in different forms: (1) basic emotions, those that are probably universal and involve less cognitive complexity for example anger and fearfulness, appear primarily in evolution and biology; and (2) emotion schemas, that include cognitive components differ across individuals and cultures^[44,45].

Basic emotions usually occur in acute situations and easily bypassing cognitive process in favor of a quick reaction to the situations. Emotion schemas are emotions that have been interpreted by the cognition.

Past experience and emotion

Experience is emotional historical facts, similar perhaps to a textbook of history that is none other than a compilation of factual events. Without emotions, every life experience would be reduced to none others but a talking history textbook. There are no memories without emotions just as there are no persons without experience. Past experience becomes memory because of the emotional content it carries. Accumulated past experience influences personality and personal belief systems in an individual^[46], and shapes the cultural behaviors in the family and community^[47]. The flavor of these memories depends on personal interpretation of the meanings of the experience. Although the objective events would arouse universally similar emotions, its unique interpretation will lead to different meanings for the person experiencing them. This is where the effect and influence of cognition comes in. Thus, emotions serve like a repository for learned influences, possessing certain invariant features and show considerable variation across individuals, groups, and cultures^[48].

These past experiences, crystalized as emotions, facilitates learning and motivates preparedness for future interactions with people, events, and situations. Evidence indicates that experimentally facilitated formation of emotion-cognition interaction i.e. schemas (such as simply learning to label and communicate about feelings) generates adaptive advantages^[49,50]. The dynamic interplay of emotion and cognition determines many human behaviors, for example connecting appropriate cognition to feelings increases the individual's capacity for emotion modulation and self-regulation^[49]. The first step towards initiation of action is by improving the perception of emotions that entails the registration of emotions in the consciousness. This is made possible by the ability to symbolize feelings and put them into words thus providing an empowerment for emotion regulation, influencing emotion-cognition relations and developing high-level social skills. Without this, the unlabeled, unarticulated, and linguistically inaccessible emotional feelings would be in the phenomenal consciousness or some other cognitively inaccessible level of consciousness although it can still be felt and functions as a mediator of behavior, retaining its motivational and informational qualities^[49].

EMOTION AND COGNITION

Emotion alone could never be the sole mediator of personally or socially significant behaviors. Other persons and contextual variables do also contribute to the causal processes of certain behaviors. However, it is proposed that emotion is always one of the mediators of a behavioral action in response to basic emotion and a mediator

of thought and action in response to emotion schemas^[40]. Therefore, the specific impact of emotions in generating and altering behavior depends on the type of emotion involved in the causal process. In basic emotions, feelings affect action but not higher-order cognition, which has little influences in the basic emotion processes. In contrast, feeling in emotion schemas may frequently effect action through its effect on the cognition. Hence, thinking becomes a key agent in regulating and guiding behavior that arises from the emotion schemas^[51].

A cognitive appreciation of emotions in relation to the issue or event at hand turns out to be the actual initiator of decision-making. In other words, a person agrees to do an action because he or she feels right and happy about the intended action, and apply controlling power over or drawing its motivation from the emotions. The direction of this decision could be at its best instinctive (without cognitive appreciation-the basic emotions^[44]) and primitive (the emotion schema^[44]). If it is not based on and guided by higher moral value. This higher value system is closely related to the concept of purpose in life in many resilience studies^[52-54]. This higher value could arise from the self-generated value system (close-system) or be imparted from the supreme beings or religion-based value system (open-system)^[55]. These three tiers of the action-sources in the interplay of the emotion-cognition-higher value system could distinguish between hot (impulsive), cold (ordinary) and extra-ordinary men, respectively.

EMOTION, COGNITION AND BEHAVIOR

The current perception is that emotion remains primarily about motivation^[56], while cognition (particularly about goal concepts that typically have an emotive component) remains primarily about knowledge. The presence of both is almost always the case in any normal human being for his or her normal social functioning^[57]. However, they could differ in sequence of activation and intensity depending on the stage of life and situations the person is in^[57,58]. The presence of both the emotion and cognition is invariably necessary for adoption of new life skills and adaptation to new environments^[59].

Emotional intensity theory suggests that emotions have motivational properties because they furnish energy and direction for the execution of appropriate instrumental behaviors^[60,61]. Specifically, emotions promote fast adaptation to situational demands by helping individuals to identify relevant and important events and by urging, guiding, and maintaining the behaviors necessary for dealing with these events^[48,60]. For instance, if someone is insulted and experiences anger, all biological systems and resources are coordinated so that the person can deal efficiently with the situation while ignoring all other signals and events. Thus, affective systems are designed to conserve energy and mobilize resources to achieve a short-term goal. These emotions are typically short-lived psychological-physiological phenomena that represent

efficient adaptations to the demands of the changing environments. Psychologically, emotions activate relevant associative networks in memory, which alter attention and shift certain behaviors upward in the response hierarchies. Physiologically, emotions rapidly excite and orchestrate the responses of various biological systems, including the autonomic nervous system activity and endocrine activity, to produce a bodily milieu that is optimal for effective response. The manifestations include facial expression, somatic muscular tonus and voice tone. Therefore, over longer periods of time, with many of these emotional encounters, people mature through the ages^[62], emotion-enriched experiences serve to establish our position in our environment, drawing us toward certain people, situations, objects, actions and ideas, and pushing us away from the others.

Because emotions are viewed as motivational states, their intensity should be effected by factors similar to those influencing the intensity of regular motivational states^[61]. Events that interfere with the experience of an emotion can influence the intensity of that emotion. Past work has shown that emotional intensity was similar to motivational arousal, which could be jointly influenced by the importance of a goal and the difficulty of achieving it^[61]. In the case of anger, events that interfere with feeling or expressing anger can affect its intensity.

The interaction between emotions and cognition in decision-makings has also been reported where emotion, in particular worry, has been shown to cause more short-term decision (cognition domain) over long-term choices that may have significant consequences to health^[63]. Emotional regulation *via* cognition such as cognitive re-appraisal and expressive suppression are shown to lead to better social adjustment, mental health and overall well-being^[64]. Furthermore, cognitive training in patients with psychiatric disorders (schizophrenia, attention deficit hyperactivity disorder, mood disorders and substance use disorders) could improve emotional regulation, clinical symptoms, and adaptive community functioning^[65]. This concept of emotional regulation as related to willpower elaborated below is invariably associated with physical health too.

Self-regulation

Self-regulation has its major explanatory mechanism in social cognitive theory^[66]. Self-regulation that is effective results in execution of a behavior and suppression of another competing but undesirable behavior. It begins from having a valued personal standard on certain actions or behaviors, which would then generate heightened motivation in realizing the action-behavior. Execution of certain actions or new behaviors is sometime aided by proactive consideration of the possible effect or consequence of the current actions-behaviors in the future, or evaluative reactions of others towards one's behavior. Self-monitoring of performance would compare the outcomes of the performance to social or personal past referential achievement^[66]. Without comparison to

the valued extrinsic outcomes, there would be absence of meaningful feedback that could in turn activate self-evaluative motivators.

Psychological functions described by self-regulation include components of self-discipline, self-reactive influences and self-gratification^[66]. It is presumed that the common values or motives within every individual are beneficial, self-constructive, pro-social and respectable. There are no objective universal referent standards that every individual could subscribe to besides those that are subjective and internal within that individual, and those that are external on the society or significant others at large. This socio-cognitive functioning of self-regulation in decision making for or against certain action learn from past experience of exercising control over the dynamic environment. Through this repeated process, conceptual skills become acquired skills and self-efficacious^[66].

Overt self-centeredness of this theory predisposes to self-love at best and despondency or depression at worst from dysfunctional self-regulation as a result from misperception on performance standards and misjudgments on achievement of self^[66,67]. It is a closed system that could suffer from inconsistency of the internal standards as compared to the more universal moral standards^[68]. As a result, it would also suffer from a sense of helplessness and hopelessness^[69] from devoid of the ultimate source (supreme beings or God in the open-value system) of help and hope in the face of weakened coping efficacy and beliefs which is highly possible in many chronic diseases self-care failures such as in patients with DM. This external source of the internal reserve may enable a self-renewal for a new beginning of coping with life challenges. Hence, it is not impossible that religiosity and spirituality could affect glycemic control^[70].

Self-efficacy

Self-efficacy is embedded within the theory of self-regulation^[66]. It operates as one of the main proximal determinants of self-regulation though self-monitoring, goal setting and valuation of activity sub-functions. Self-efficacy is self-confidence or self-believe in one's own ability to carry out or overcome difficulties inherent in specific tasks^[71]. Hence, beliefs of one's own efficacy cause people to make choices, aspire and persevere in things that they have the confidence in achieving. This theory suggests that people with higher self-efficacy would keep improving in life due to their positive self-feedback and setting higher new targets to achieve in progressive efforts.

This confidence stems from learned capability gained through past experiences when efforts were expended for the behaviors^[72]. In this theory, differential experience and cognitive processing of efficacy information lead to different degree of self-efficacy attainments. The intervening link between the efficacy expectation and the actualization of efficacy in action could be self-aiding thoughts, the emotion-motivation fortified resilience that is powered by the activated personal value or belief system. However, similar to its parent theory of self-

regulation, self-efficacy theory relies too heavily on self-centeredness, autonomous judgments and could result in both extreme ends of self-destruction, *i.e.*, over-confidence and self-despair.

Willpower

Willpower functions like an "actualizer" of the formed intentions into real behaviors^[73]. It employs conscious and effortful self-control when faced with life choices or temptation and manifests as an ability to resist short-term gratification for long-term return^[74]. With willpower, people overcome "hot" emotional pushes with the "cool" cognitive capacity^[73]. Thus, willpower is an educated spirit that grows on understanding and has the ability to control emotions. Willpower is likened to a trait as evidenced by studies demonstrating that the similar quality of the willpower that appeared in the preschoolers persisted into adulthood^[75,76]. Past studies show that willpower was positively correlated with many aspects of life such as better academic achievement in schools, higher self-esteem, lower substance abuse rates, greater financial security and improved physical and mental health^[75,77].

The effects of willpower could however deplete if it is repeatedly exerted within a short span of time and thus is predisposed to failure of self-control in an immediate next challenge^[78]. Thus, willpower depletion is best avoided by focusing on one task at a time as it has been observed that willpower fares optimally when it is applied on one valued goal after another instead of multiple resolutions at once^[79]. This will negate the impact of willpower failure on a range of potential challenging behaviors such as food intake, substance use and abuse and purchasing behavior^[80-82]. Elsewhere it has been shown that people with positive moods, motivation, beliefs and attitudes or vitality were found to be more able to mitigate this depletion and to persevere even when their willpower strength has been depleted^[83-85]. Thus, positive emotions bolster willpower when it is weak but negative emotions, on the other hand, could be suppressed by the willpower when it is cognizant in according to the situations. Interestingly, it was noted that willpower resembled resilience in that regular exertion of self-control improved willpower strength over time^[86].

Resilience

Resilience is defined as an individual's capacity to maintain psychological and physical well-being when faced with adverse life events by drawing on self-esteem, self-efficacy, self-mastery and optimism as resources^[52-54]. Other qualities of resilience include internal locus of control, social support and purpose in life^[87]. These personal qualities vary among different individuals depending on whether the events are perceived as stressful, a threat or a challenge^[88]. Resilience has been shown to contribute to relatively successful social functioning in the elderly with DM, with an effect that was stronger than social support and material resources^[89].

It has often been a phenomenon that adversity breeds

resilience as in the analogy of a well rooted strong tree growing up in the wilderness. In man, brief and graded exposures to stressors in turn would allow cumulative experience, learning and strengthening of a person (the steeling effect)^[90-92]. Thus, there is no true resilience in the absence of true adversity^[90]. External adversity makes assessment of resilience comparable across individuals. Hence, subjective interpretation of internal adversity (such as in sickness) is acceptable as the adversity is being faced by an individual with his or her own unique socio-bio-logic milieu.

Behaving resiliently is only possible if there are reserves and resources to draw from. Reserves are internal strength of the person which when tested in the face of adversities, could either manifest in positive emotions (hope, optimism, happiness and vitality) or in negative emotions (apathetic, feel guilty, overwhelmed, disgruntled and depressed). Resources are external supports of all possible forms from every potential party. Between these two, reserves would be a closer and stronger resilient factor for simply being a more personal characteristic in the face of almost all adversity because no adversity is an adversity if it does not affect at the personal level and demand a personal response. This internal reserve depends largely on the personal value and belief system that could result from the past experience (emotional learning), educated cognition (knowledge) or relationship with a supreme being(s)^[55,87,88]. The inter-play and effectiveness of each of these factors would have manifestations that mirror the three tiers of human-action or behaviors namely; the beast-like reflex action, the ordinary but superficial culture and politeness; and extra-ordinary self-sacrificial altruism. The great divide between these factors would be the self-dependency in the former two and depending on the supreme-value or being God-dependent in the last. This divide is not necessarily mutually-exclusive but perhaps reflective of a responsible, balanced and appropriate execution of dependency on self and supreme beings or God. The greatest danger of self-dependency is probably self-deception resulting from misperceptions and self-isolation; while supreme-value or God-dependency could be far reaching for the majority, as the supreme beings/God are/is too abstract to be real as in the demand of religious faith^[55].

Illness perception

Illness perceptions involve beliefs, cognitive and emotional representations or understandings that patients have about their illness^[93]. These perceptions have been found to be associated with health behaviors and clinical outcomes, such as treatment adherence and functional recovery^[94]. Illness perceptions constitute beliefs on the chronicity of the illness, locus of control of the illness and efficacy of treatments; it includes an assessment on the perception of understanding the patient has of the illness; illness perception evaluates the emotional impact of the illness directly and indirectly from the aspects of symptoms experience and concern for the illness's conse-

quences.

Some of these illness perception dimensions had small significant associations with HbA1c^[95]. Tentative evidence indicate that illness perceptions can be positively changed through targeted intervention and that could have an impact on glycemic control^[95]. Patients' perception of their illnesses and related symptoms and their beliefs about the possible consequences of the disease had also been shown to be associated with their satisfaction with medical consultation and healthcare utilization, respectively^[96]. Misperception could complicate reassurance^[96] from healthcare professionals and impede self-coping on patient's part^[94].

Proactive coping

Future-oriented thinking or the proactive coping concept goes a step further in explaining how people could maintain an acquired behavior^[97]. In this model, a person who practices proactive coping is said to be in continual anticipation of the potential barriers and threats to the lapses of the desired behavior; have the ability to develop and realize the strategy to offset the threats. In addition to the effective use of resources, the person who is successful in maintaining his or her behavior would also use effective feedback on self-strategy to keep the goals viable. In a study of newly-diagnosed DM patients, proactive coping was shown to be a better predictor of long-term (at 12 mo) self-management (diet and physical activity and weight loss) than either intentions or self-efficacy^[98].

However, it is proactive coping rather than future-oriented thinking that seems to be more feasible and in line with other health behavior concepts. Knowing the immense possibilities of the distant future and demands of the present in self-management coping for DM might overwhelm the emotion and crumble the present functioning of a person. Applying proactive coping even for near proximal outcomes may require high degree of support, emotional and cognitive agility to succeed^[99]. Hence, patients with adequate cognitive and emotional resource and reserve would likely to cope proactively^[100]. Issues remain in individualization of such behavior, matching its intensity to the patient's characteristics and valued goals in life in order to preserve acceptable level of quality of life. Therefore, patients who can behave and cope proactively are those who have a right illness perception (right understanding about DM), perceive its importance in their life, have self-efficacy and able to self-regulate.

NEGATIVE PSYCHOLOGICAL EFFECTS ON DIABETES MELLITUS

In adults, children and adolescents with DM, depression was related to poorer glycemic control, a range of diabetes complications, increased health care costs, worsened functional disability, re-hospitalization and early mortality^[101]. Those with psychological distress at the time of diagnosis had a higher risk of cardiovascular events

(1.7-fold) and death (1.8-fold) than those without psychological distress^[102].

Emotions and the brain in DM

Current research suggest biological changes in the brain of patients with DM. Structural, functional, and neurochemical changes in the brain regions responsible for affect and cognition may have increased the risk of depression in both type 1 and type 2 DM^[103]. Animal models have shown that hyperglycemia negatively affect hippocampal integrity and neurogenesis, reducing neuroplasticity and contributing to mood symptoms^[104]. In humans, hippocampal neurogenesis and hippocampal atrophy has been observed in people with DM, which will lead to difficulty in learning, maintaining memory and governing emotional expression^[104].

Emotions and systemic inflammation in DM

In a recent published study in United Kingdom^[10], depressive symptoms in adults with newly diagnosed type 2 DM, after adjusting for covariates, were associated with systemic inflammatory markers: C-reactive protein ($B = 0.13$, $P < 0.001$), interleukin-1 β ($B = 0.06$, $P = 0.047$), interleukin-1RA ($B = 0.13$, $P < 0.001$), monocyte chemoattractant protein-1 ($B = 0.11$, $P = 0.001$), white blood cell count ($B = 0.13$, $P < 0.001$), and triglyceride ($B = 0.10$, $P < 0.001$).

The effect of negative affect and moods on the inflammatory markers, immune systems and endothelial functions are further compounded in patients with DM^[105]. This is because hyperglycemia in diabetes has already deleterious effect on the endothelium^[106,107]. The “glucose tetrad” of HbA1c, glycemic variability, fasting and postprandial plasma glucose activate oxidative stress causing vascular complications through endothelial dysfunction and damage^[108]. Chronic glycation of mitochondrial respiratory proteins leads to mitochondrial DNA damage and functional decline causing over-production of intracellular free radicals and perpetual cellular injury^[109]. Non-enzymatic glycosylation of other proteins and lipids by disrupting their molecular conformation alter many enzymatic activities, reduce degradative capacity and interfere with receptors recognition^[110]. The presence of hypertension and hyperlipidemia in patients with diabetes impose added detrimental effect on the micro- and macrovasculature. These include cholesterol oxidation and glycosylation contribute to the progression of atherosclerosis by promoting vascular smooth muscle cells migration and proliferation^[111]. In the hypertensive diabetes patients, impaired auto-regulation in the micro-circulation with non-dipping of nocturnal blood pressure leading increased pulse-wave velocity, ventricular-vascular mis-coupling and premature stiffening of the abdominal aorta owing to autonomic dysfunction and elastic fibres glycation^[112].

Emotion lability and biomarkers variability

It is widely observed that emotions are relatively stable

over time, constitute the person general outlook and represent personality. However, it is possible that affects change from time to time. It was reported that changes in affects and emotions over a short period of time were detrimental to health, especially in the cardiovascular organ systems through the sudden or unpredictable surge in pulse rate and blood pressure^[22,113]. Dysregulation of emotions can impact on physical health through the autonomic nervous system activation and hypothalamic-pituitary-adrenal axis activation that affect the metabolic and immune functioning of a person^[11,23,24,27,28]. Therefore, it is hypothesized that unregulated emotional fluctuation could lead to variability in blood pressure and glycemic control biomarkers. In the reverse direction, Penckofer^[114] had reported that glycemic variability measures were associated with mood (depression, trait anxiety and anger) and quality of life. The 24-h SD of the glucose readings and the continuous overall net glycemic action measures were significantly associated with health-related quality of life (HRQOL) after adjusting for age and weight; and subjects with higher trait anxiety tended to have steeper glucose excursions.

In patients with DM, a recent Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation trial had reported clear associations between visit-to-visit variability (VTV) of HbA1c and the risk of macrovascular events ($P = 0.02$ for trend), whereas fasting glucose variability was associated with both macro- and microvascular events ($P = 0.005$ and $P < 0.001$ for trend, respectively)^[115]. In an earlier study it has been shown that HbA1c variability affects nephropathy more than average HbA1c, whereas only the latter parameter affects retinopathy^[116]. On the other hand, glucose variability as characterized by extreme glucose excursions, independent of HbA1c levels, could be a predictor of diabetic complications (development or progression of diabetic retinopathy and cardiovascular events) and mortality in patients with DM^[117]. The mounting evidence on these associations suggest that increased frequency and magnitude of glycemic variability generates more reactive oxygen species that triggers the various metabolic pathways of glucose-mediated vascular damage which result in an increased risk for the development of long-term diabetic complications^[118,119].

Similarly, VTV in systolic blood pressure (SBP) and maximum SBP are strong predictors of stroke, independent of mean SBP^[120]. Increased residual variability in SBP in patients with treated hypertension was associated with a high risk of vascular events^[120]. In each TIA cohort, VTV in SBP was a strong predictor of subsequent stroke (top-decile hazard ratio over seven visits: 6.22, 95%CI: 4.16-9.29, $P < 0.0001$). In ASCOT-BPLA^[121], residual VTV in SBP on treatment was also a strong predictor of stroke and coronary events (top-decile HR for stroke: 3.25, 2.32-4.54, $P < 0.0001$), independent of mean SBP in clinic or on ambulatory blood pressure monitoring (ABPM). Variability on ABPM was a weaker predictor, but all measures of variability were most predictive in

younger patients and at lower ($<$ median 142.8 mmHg) values of mean SBP in every cohort^[120]. However, there is no evidence to date that suggest similar detrimental effects of cholesterol variability in adult patients with DM.

PSYCHOLOGICAL INTERVENTION IN DIABETES CARE

Despite evidence that psychosocial support was instrumental to adaptive self-care as indicated by patients in the DAWN2^[6], psychosocial and pharmacologic interventions have not been widely used to target psychological co-morbidities such as depression and DRD^[122]. The psychosocial supports through caring and compassionate family, friends, health care professionals, and even other patients with DM could instill a positive outlook, sense of resilience and wellbeing in patients with DM. Screening, evaluation and management of psychological disorders such as depression and DRD in people with DM in primary care are feasible^[123].

Indeed, positive psychosocial factors are important mediators or independent predictors of clinical outcomes in chronic diabetes care and positively related to self-care behaviors^[124], exerting a direct impact on HRQOL and subjective health. A recent review^[125] and study^[126] reported that positive emotional health (well-being, positive affect, resilience and gratitude) were linked to self-management (exercise, treatment adherence and frequency of blood glucose monitoring), health-related outcomes (HbA1c, health status and HRQOL) and lower risk of all-cause mortality in patients with DM^[3,125]. However, few quality studies have investigated the effects of positive aspects of emotional health (resilience, positive affect, well-being) on patient outcomes; even lesser empirical studies showed strong evidence of the actual effect of positive and negative affect on glycemic control^[127,128]. Although the interaction between emotional health and diabetes physiology and patient's self-care practices that in turn further influence health outcomes are becoming clearer, there is still a paucity of health programs that incorporate human psychology wholesomely and intervene effectively in patients with DM for improved self-care behaviors and clinical outcomes^[129,130]. Some recent studies that examined depressive symptoms and DRD and their management has found cross-sectional, prospective and time-concordant relationships with HbA1c^[131,132]. Nevertheless, a causative relationship between the two requires more significant prospective linkages between DRD and HbA1c^[132]. From the discussion above, it is possible that emotional disorders can affect HbA1c in a bidirectional pattern^[133]; from distress or depression to DM *via* lifestyle factors and due to therapeutic demands in the reverse direction^[133].

Notwithstanding, interesting questions emerge whether interventions involving psychological, intra- and interpersonal resources may be possible to buffer the negative inflammatory effects of emotional disorders in patients with increased risks of cardiovascular diseases such as in

patients with DM. Improving cognitive appreciation in education, increasing positive affect and motivation to initiate positive lifestyles could in turn lead to better self-care behavior and quality of life. Therefore, interventions that focus on positive emotional health to diminish negative emotions could enhance health in part through their positive impact on immune and endocrine regulation, resilience, self-efficacy, positive behaviors and HRQOL^[34].

The immediate next questions would be: (1) How much of these effects could be achieved in patients and within their family members? (2) How personalized should the interventions be? and (3) How much do the existing health systems need or able to transform in order to implement the interventions? These questions consider other potential social determinants of DM that may influence effectiveness in diabetes care provision^[134]. The first question involves the essential issue of the characteristics of patients in participating the interventions for example their pre-intervention health beliefs and barriers to change assuming the interventions that follow would help them to put right most if not all health beliefs and behaviors. The second question involves having cost- and content-effective interventions^[135,136] that may need to be separately prepared for patients at different stages of diseases for example newly diagnosed DM, persistent poor control of disease, impending or newly diagnosed complication/comorbid; or going into different life stages such as young working adults, family planning or pregnancy, retirement and above 60-year-old^[137]. The personnel to deliver the interventions will need training that would enable them to conduct a flexible, dynamic and culturally appropriate interventions^[136,138,139]. The third question implies staff and health system readjustment and investment to begin the intervention^[140,141], to maintain and even to continuously update the interventions in accordance with the contemporary evidence of medicine^[142]. The ultimate aims would be to help individual patient to develop own strategies for the long-term management of their diabetes, and that at the same time leading a productive life resulting from a quality of life that is resilient to adversities and challenges.

CONCLUSION

Understanding the nature of the psychological aspects that are pertinent in patients with DM, and the links between the emotional disorders (stress, distress, anxiety, DRD and depression) and inflammation has provided a mechanistic insight into the relationships between psychological domains and poor physical health^[34]. Positive emotional health may sustain long-term coping efforts and protect patients from the negative consequences of prolonged emotional disorders^[143], illness perception and thus facilitating diabetes self-management behaviors and better physical health. Having patients acquire valued personal beliefs and achievable standards of performance could strengthen self-regulation and self-efficacy and lead to more positive experience and healthy behaviors.

Furthermore, improved personal resources such as resilience would lead to better functioning of cognition and stronger willpower, quality of life and disease control in patients with DM. More research is needed to understand what factors contribute to individual DM differences in vulnerability, treatment response and resilience to psychological disorders and cardio-metabolic risk factors control across the life course. More international collaboration is helpful to examine how best to provide care for people with DM and emotional disorders in different health care and cultural settings. Psychological training programs grounded on sound theoretical framework such as that draw on the fundamental value system or personal purpose in life could effect powerful involvement of emotion and cognition leading to meaningful and lasting behavioral change. Lastly, a cross-disciplinary workforce is necessary and the program should be culturally flexible for it to work in different models of healthcare system and for patients with DM of different backgrounds^[101].

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