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Disaggregating diabetes

New subtypes, causes, and care

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Abstract

Interest in disaggregating diabetes into numerous subtypes is growing as patients and providers recognize the limitations of standard diabetes typologies. As anthropologists, we draw attention to how ‘subtyping’ may reduce stigma derived from the connection between obesity and ‘type 2 diabetes’. We highlight the complexities that drive diabetes and argue that an exclusive or dominant focus on diet and obesity obfuscates other underlying risks. Yet, we warn that subtyping may promote unnecessary pharmaceuticalization, especially for other subtypes of diabetes that may be associated with stress and inflammation. We call upon providers to continue to closely attend to patients’ lived experiences. While we recognize the shortcomings of the existing classificatory scheme, patients’ outcomes and prognoses are often more closely connected to the social and medical support they receive than to the underlying metabolic classification.

Keywords

diabetes, typology, classification, medicalization, global health

‘Am I type 5 today?’, asked a woman seeking care for her diabetes in Xela, Guatemala, a decade ago. ‘Oh, no, that’s not how it works’, the nurse responded. The nurse’s answer reflected medical knowledge about diabetes at the time, but today there seems to be truth in the patient’s question. Emerging research suggests that diabetes has multiple, locally variant, and unstable typologies. This departs from the common understanding of three distinct types of diabetes (type 1, type 2, and gestational diabetes). ‘Subtyping’, defined as the production of different types of diabetes, can usefully identify diverse manifestations of an enigmatic disease, with the promise of more sensitive courses of treatment and prevention (Ahlqvist et al. 2018; Dahl et al. 2019; Li et al. 2019; Tuomi et al. 2014; Udler et al. 2018). However, as we discuss here, subtyping must incorporate the social and psychological dynamics that shape diabetes presentations and prognoses.

The interest in subtyping reflects a turn toward what is called ‘precision medicine’: the customization of disease management and a corresponding presumed improvement in outcomes. Beyond monogenic subtypes such as latent autoimmune diabetes of adulthood and forms of secondary diabetes, a new array of subtypes has been identified statistically, through data-driven cluster analyses of genetic variance, clinical factors (such as age at diagnosis, BMI, and insulin resistance), and the development of complications over time. For example, Udler and colleagues (2018) identify five diabetes subgroups: a ‘beta cell cluster’, a ‘proinsulin cluster’, an ‘obesity cluster’, a ‘lipodystrophy cluster’, and a ‘liver/lipid cluster’, all differentially associated with clinical outcomes. Most analyses of cluster-related data have been conducted in wealthy nations (Ahlqvist et al. 2018; Dahl et al. 2019; Li et al. 2019; Udler et al. 2018), although evidence from China also suggests subtype variation (Tuomi et al. 2014). Where investigators have not derived clusters to directly account for genetic variance, they point to genetic variation as key (Ahlqvist et al. 2018; Lin and Wessel 2019).

However, refining diabetes subtypes along genetic lines ignores social and environmental effects on etiology and treatment outcomes. For example, the increased detection of diabetes in sub-Saharan Africa and South Asia among people who are thinner and younger (International Diabetes Federation 2015) may reflect subtypes that are not linked to obesity in adults, but these populations are traditionally excluded from genetic studies. Ethnographic research among people who have experienced chronic medical insecurity, food insecurity, and humanitarian crisis shows that the combined effects of trauma and stress produce contingent expressions of diabetes that complicate the type 1–type 2 binary (Carruth and Mendenhall 2019; Moran-Thomas 2019). Somali diabetes patients, for instance, demonstrate unexpected but distinct clinical presentations, including progressive nutritional wasting, weakness, and dental disease, despite therapeutic compliance (Carruth and Mendenhall 2019).

Studies find intergenerational links between stress and diabetes (Thayer and Kuzawa 2011), as well as links between stress and diabetes across an individual's life course. For instance, the Barker hypothesis suggests that maternal nutrition and body weight influence generational patterns of cardiometabolic risk (Barker 1999; Barker et al. 1989). The influential Developmental Origins of Health and Disease model of intergenerational effects on health outcomes also illustrates the importance of environmental triggers early in life (Gluckman and Hanson 2004). Others point out that developmental plasticity and epigenetic changes continue well beyond early life (Colom 2015; Pentecost and Ross 2019; Warin and Zivkovic 2019). Diabetes also may be linked to trauma in childhood (Felitti et al. 1998), affecting the body via dynamics of cortisol and insulin production (Henley et al. 2013), and in the bidirectional relationship between depression and diabetes (Holt, Groot, and Golden 2014). The role of acute and chronic distress in diabetes, and potential genetic factors of this distress, remains a constant theme across different subtypes.

The pharmaceutical industry plays a significant role in producing, refining, and treating new diabetes subtypes. Industry representatives sit on the American Diabetes Association (ADA) board and inform treatment recommendations; this includes lowering thresholds for the hemoglobin A1c test (a common diabetes diagnostic test that shows a person's average blood sugar over the last two to three months) to determine who needs medication (Choudhry, Stelfox, and Detsky 2002). Critics have argued that the expansion of the ADA's category of 'prediabetes', based on these lower A1c thresholds, reflects industry influence, rather than a demonstrated benefit of such a diagnosis in improving population-level diabetes prevention (Kivimäki and Tabák 2018; Yudkin and Montori 2014; Vasquez 2018). Increasingly complex prescription regimens target different metabolic systems and pathways, but not all subtypes may need medication. Prescribing psychotherapy, group counseling, or community-based approaches to address emotional and social distress may improve patient outcomes and reduce cascading side effects of multiple drugs (Musselman et al. 2003).

The expansion of subtypes has sociocultural and clinical significance. Type 2 diabetes treatment strategies have long relied on blaming and shaming individuals for their 'lifestyle' choices (Yates-Doerr 2011). People whose diabetes does not respond to clinical guidance to eat healthier diets and to exercise more frequently are classified as 'bad patients' (Naemiratch and Manderson 2006). Subtyping may have a desirable effect of destigmatizing those who do not 'adhere' to these clinical recommendations because it may indicate a different subtype that requires nonmedical interventions (such as counseling). This may reduce stress among those who face challenges accessing healthy foods and safe places to exercise, dealing with family and work pressures, managing the demands of preparing separate meals, and executing complex treatment regimens. Subtyping may, however, have the harmful effect of

prioritizing concern for ever-greater diagnostic specificity at the expense of strengthening social networks of aid and care.

As interest in subtypes and subtyping grows, lived experiences of diabetes and its typologies require attention in our research and recommendations. The social and economic conditions that shape all types of diabetes are fundamental to determining insulin resistance, response to medications, and whether and when complications develop. Genetic explanations of typologies should not divert attention from the structural inequalities and interpersonal dimensions of diabetes. We must also resist the individualization of diabetes disparities: patients' outcomes and prognoses are often more closely connected to the social and medical support they receive than the underlying metabolic classification.

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