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The Borderline Effect for Diabetes: When No Difference Makes a Difference

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Scope Statement

Presents original research and preliminary findings of a borderline effect among people without meaningful initial differences in A1c blood test results that become meaningful in the direction predicted by the label.

Conflict of interest statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest

CRediT Author Statement

Ellen Langer: Conceptualization, Writing – review & editing. Peter James Aungle: Conceptualization, Formal Analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing.

Keywords

diabetes, diagnostic labels, Self-fulfilling beliefs, perceived risk, Perceived control

Abstract

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We hypothesized that people at the borderline of being labeled as "prediabetic" based on A1c blood test results, who initially face equivalent risks of developing diabetes but who are labeled differently, would be more likely to develop diabetes when labeled as "prediabetic."Study 1 surveyed 260 participants on Amazon Mechanical Turk to test whether risk perception significantly increased when comparing A1c test results that differed by 0.1% and led to different diagnostic labels (5.6% and 5.7%) but did not significantly increase when comparing those that differed by 0.1% but received the same label (5.5%/5.6% and 5.7%/5.8%). Study 2 explored whether labels are associated with different rates of developing diabetes when the initial difference in A1c results suggests equivalent risk. Using data from 8,096 patients, we compared patients whose initial A1c results differed by 0.1% and found those who received results labeled as prediabetic (A1c of 5.7%) were significantly more likely to develop diabetes than patients whose initial results were labeled as normal (5.6%). In contrast, patients whose initial results differed by 0.1% but who received the same "normal" label (5.5% and 5.6%) were equally likely to develop diabetes. These preliminary results suggest that diagnostic labels may become self-fulfilling, especially when the underlying pathology of patients receiving different labels does not meaningfully differ.

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Studies involving animal subjects

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Studies involving human subjects

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Inclusion of identifiable human data

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Data availability statement

Generated Statement: The datasets presented in this article are not readily available because we do not currently have permission to share the retrospective patient data from Tufts Medical Center. We are happy to share the data from Study 1 and can seek approval to share the retrospective data with approved third parties.. Requests to access the datasets should be directed to peter_aungle@fas.harvard.edu.

The Borderline Effect for Diabetes: When No Difference Makes a Difference

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Abstract: We hypothesized that people at the borderline of being labeled as "prediabetic" based on A1c blood test results, who initially face equivalent risks of developing diabetes but who are labeled differently, would be more likely to develop diabetes when labeled as "prediabetic." Study 1 surveyed 260 participants on Amazon Mechanical Turk to test whether risk perception significantly increased when comparing A1c test results that differed by 0.1% and led to different diagnostic labels (5.6% and 5.7%) but did not significantly increase when comparing those that differed by 0.1% but received the same label (5.5%/5.6% and 5.7%/5.8%). Study 2 explored whether labels are associated with different rates of developing diabetes when the initial difference in A1c results suggests equivalent risk. Using data from 8,096 patients, we compared patients whose initial A1c results differed by 0.1% and found those who received results labeled as prediabetic (A1c of 5.7%) were significantly more likely to develop diabetes than patients whose initial results were labeled as normal (5.6%). In contrast, patients whose initial results differed by 0.1% but who received the same "normal" label (5.5% and 5.6%) were equally likely to develop diabetes. These preliminary results suggest that diagnostic labels may become self-fulfilling, especially when the underlying pathology of patients receiving different labels does not meaningfully differ.

Keywords: diabetes, diagnostic labels, self-fulfilling beliefs, perceived risk, perceived control

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Introduction

Two marathon runners are nearing the end of a marathon. One notices that they are just over 3 hours and 52 minutes into the race with about a mile to go (a pace of around 9 min/mile). They pick up their pace for the final stretch and finish in just under 4 hours. The other runner notices that they are around 3 hours and 55 minutes into the race with three quarters of a mile to go. They quickly calculate they would need to run significantly faster than they had been and feel fatigued by the thought. They slow down and end up finishing in 4 hours and 5 minutes. Pick any marathon, and if one looks at a distribution of finish times, they will invariably find a spike just under 4 hours that quickly falls off after the 4-hour mark. Being someone who finishes marathons in under 4 hours apparently motivates runners on the borderline to pick up their pace. But when that positive label is perceived to have fallen out of reach, the extra motivation dissipates and can even reverse [1]. Such is often the effect of labels: they influence how we make sense of experience and consequently shape behavior, affect, and physiology [2; 3; 4; 5; 6; 7; 8; 9].

In the studies described below, we sought to answer a simple question: given two patients with nearly equivalent results on a diagnostic test, but who differ enough to warrant different diagnostic labels, what, if any, are the effects of the label? With any continuous variable that has been divided into different categories based on certain thresholds, the borderline between categories becomes increasingly less meaningful the closer the results are to the borderline [10]. The motivation for the studies described below was to test the effect of diagnostic labels on health trajectories and outcomes by comparing cases in which initial diagnostic labels suggested different risks but the underlying test results did not. We focused on the diagnostic labels used to identify individuals at risk of developing type 2 diabetes. Diabetes diagnoses have almost

quadrupled globally over the past three decades, making diabetes one of the most important international public health challenges, affecting more than 460 million people and costing nearly $760 billion globally in 2019 alone [11; 12]. Ninety percent of diagnosed diabetes cases are considered type 2, in which the body fails to generate sufficient insulin or fails to use it properly [13].

Given the potential short-term and long-term complications that can result from diabetes – including strokes, neuropathies, kidney disease, and vision problems [14] – it is noteworthy that psychological influences appear to shape the physiology of the illness. For example, stress has been consistently associated with higher blood glucose levels among nondiabetics and diabetics alike [15]. Similarly, depression [16], and psychological comorbidities more generally [17], negatively affect diabetic physiology. Some of the most interesting evidence that psychological influences alone can shape diabetes-related physiology comes from studies that found blood sugar levels followed perceived time, independent of actual time [18] and perceived sugar content, independent of actual sugar content [19]. Collectively, these findings provide compelling evidence that psychological factors shape the underlying pathology characteristic of type 2 diabetes.

In this paper, we first studied whether the perception of risk is more sensitive to changes in diagnostic labels than to underlying changes in A1c test results.

Study 1

We recruited participants to complete a survey on Amazon's Mechanical Turk that asked participants to imagine different psychological and behavioral responses to receiving A1c results that differed by the smallest possible value (0.1%). We surveyed 260 participants (175 male, average age = 40.8 years [SD = 7.54]) about how they imagined they would feel and act.

Methods

After providing informed consent, participants were randomly assigned to one of three conditions: one in which they imagined A1c test results that both corresponded to "normal" labels, one in which they imagined one "normal" result and one "prediabetic" result, or one in which they imagined A1c results that both corresponded to "prediabetic" labels. Within each condition, A1c test results were counterbalanced – half the participants saw the higher of the two results first, the other half saw the lower of the two results first. In the first group, participants imagined receiving results of either 5.5% or 5.6% (both labeled as "normal"). In the second group, they imagined receiving results of either 5.6% or 5.7% (the first was labeled as "normal," the second was labeled as "prediabetic"). In the third group, they imagined receiving results of either 5.7% or 5.8% (both labeled as "prediabetic"). For each A1c test result that participants imagined receiving, they responded to four survey items that asked them about their perceived likelihood of developing diabetes, the degree of worry they would feel, the agency they'd feel to take effective preventative action, and the efficacy they perceived in preventative medical care.

We predicted that the only significant within-group differences would occur in the second condition, in which the 0.1% difference corresponded to different diagnostic labels: "normal" vs. "prediabetic."

Measures

Risk Assessed impact of the two test results on perceived risk of developing diabetes. "Compared to most people your age and sex, what would you say your chances are for developing diabetes?" (1 = very unlikely, 6 = very likely)

Worry Asked participants to rate their concern about developing diabetes. "I would be worried about developing diabetes." (1 = strongly disagree, 6 = strongly agree)

Agency Assessed the degree to which participants imagined feeling control over the likelihood they would develop diabetes. "There's a lot I can do to prevent the development of diabetes." (1 = strongly disagree, 6 = strongly agree)

Medical Care Assessed the extent to which participants said they would believe that regular medical care would protect them from developing diabetes. (1 = strongly disagree, 6 = strongly agree)

Results

Mixed between-within-subjects linear models were constructed to test whether responses to our measures were significantly influenced by the A1c test results participants imagined receiving. The measures described above were the outcome variables, A1c score was the predictor, and correlations between repeated measures were accounted for by including a random intercept in each model.

Group 1 Participants imagined receiving two A1c test results, both of which corresponded to "normal" labels (5.5% and 5.6%). Half of the participants imagined the higher number first (counterbalanced randomly across participants). We found no differences on any of our four measures.

Group 1 | Normal Labels | N = 84				
	5.5% ("Normal" A1c)		**5.6% (Normal A1c)**	
	Mean	SD	Mean	SD
Risk	3.38	1.405	3.40	1.354
Worry	3.70	1.421	3.76	1.453
Agency	4.74	0.983	4.77	1.079
Medical care	4.45	1.186	4.50	1.197

Group 2 Participants imagined two A1c test results, one of which corresponded to a "normal" label (5.6%) and the other of which corresponded to a "prediabetic" label (5.7%). Half of the participants imagined the higher number first (counterbalanced randomly across participants). Participants perceived significantly greater risk of developing diabetes (mean difference = .556, $t(89) = 4.87$, $p < 0.0001$) and said they would worry significantly more (mean difference = .689, $t(89) = 5.15$, $p < 0.0001$) when they imagined receiving a result of 5.7% ("prediabetic") compared to when they imagined receiving a result of 5.6%. Results on our measures of perceived agency and the protective value of regular medical care did not significantly differ. In short, participants said they would be more worried but would not behave differently.

Group 2 | Label Change | N = 90				
	5.6% ("Normal" A1c)		**5.7% ("Prediabetic" A1c)**	
	Mean	SD	Mean	SD
Risk* **	3.50	1.211	4.06	1.115
Worry* **	3.69	1.196	4.38	1.250
Agency	4.67	0.983	4.66	1.018
Medical care	4.60	1.099	4.69	0.979

Group 3 Participants imagined two A1c test results, both of which corresponded to "prediabetic" labels (5.7% and 5.8%). Half of the participants imagined the higher number first (counterbalanced randomly across participants). In contrast to our hypothesis, participants perceived greater risk of developing diabetes (mean difference = .233, $t(85) = 2.58$, $p = 0.0116$) and said they would worry more (mean difference = .267, $t(85) = 2.51$, $p = 0.0139$) when they imagined receiving a result of 5.8% ("prediabetic") compared to when they imagined receiving a result of 5.7% ("prediabetic"). The more threatening label apparently increased psychological sensitivity to small differences in A1c results, but again participants did not imagine they would behave any differently.

Group 3 | Prediabetic Labels | N = 86				
	5.7% ("Prediabetic" A1c)		5.8% ("Prediabetic" A1c)	
	Mean	SD	Mean	SD
Risk*	4.01	1.232	4.24	1.04
Worry*	4.30	1.284	4.57	1.342
Agency	4.58	0.988	4.64	1.084
Medical care	4.52	1.003	4.49	1.155

Differences between groups Applying a mixed between-within-subjects linear model to test for differences across groups, the pattern of results suggests participant perceptions were dominated by the diagnostic label. Similar to the within-group differences we found in Groups 1 and 3, the model indicated a significant between-group effect on perceived risk and worry but not on agency or medical care. Pairwise contrasts with p-values adjusted using the Tukey method indicated that this effect was only significant when comparing the responses from Group 1 to those from Group 3. Participants who responded to results both labeled as "normal" perceived significantly less risk (mean difference = -0.735, $t(257) = -4.189$, $p = .0001$) and imagined feeling significantly less worried about developing diabetes (mean difference = -0.704, $t(257) = -3.778$, $p = .0006$) than did participants who responded to results both labeled as "prediabetic."

Discussion

The purpose of this study was to test whether small differences in A1c test results only result in significantly different responses when they correspond to different diagnostic labels. If participants treated small differences in underlying A1c results equivalently, differences in perceived risk and imagined concern about developing diabetes should have been similar within each group. Instead, participants in Group 1 responded as if the 0.1% difference represented an equivalent result, participants in Group 2 perceived significantly greater risk and imagined worrying significantly more, and participants in Group 3 perceived slightly higher risk and imagined worrying slightly more – the only group that appeared to respond more to the specific

A1c result than to the diagnostic label. Thus, the psychological effect of the same 0.1% difference was far from equal. When comparing results between groups, the only significant differences to emerge were from contrasting the group that only saw "normal" labels to the group that only saw "prediabetic" labels.

Study 2

In Study 1, we established that small differences in A1c results loom disproportionately large when those differences correspond to different diagnostic labels. When both results were labeled normal, the difference in the underlying result was irrelevant. When the label changed, participants perceived significantly greater risk of developing diabetes and said they would worry significantly more. When both results were labeled as prediabetic, participants perceived slightly greater risk and said they would worry slightly more if they received the higher of the two A1c results. This suggests that the "normal" label dominated judgments of A1c results in the first group; that participants in the second group were especially sensitive to small differences because they corresponded to different diagnostic labels; and that participants only began to perceive A1c results as a continuous measure of risk because both results were labeled as "prediabetic" in the third group.

In the retrospective analysis we conducted for Study 2, we tested whether the frequency with which people developed diabetes in a real-life patient population differed based on the label assigned to their initial A1c results. We partnered with the endocrinology team at Tufts Medical Center to develop the study design and to obtain retrospective data for patients whose initial lab results when they entered the system were between 5.5% and 5.8%. Our hypothesis was that A1c trajectories and the frequency with which patients developed diabetes would be significantly

worse when the initial A1c results were labeled as "prediabetic" compared to when they were labeled as "normal."

Methods

We received data from Tufts Medical Center containing: 32,957 A1c test results from 8,096 patients (3,370 men) who received initial results after the "prediabetes" label was adopted. At the time the data were extracted, the patients were 59 years old on average (SD = 11.83, IQR = 17 years). We grouped patients by initial A1c results and conducted chi-square tests within each group to compare the number of patients who developed diabetes to the number who did not.

Results

We first limited our analysis according to the design we developed in consultation with the endocrinologists who provided these data: we compared the number of "high normal" patients (initial A1c results of 5.5% and 5.6%) who developed diabetes to the number of "low prediabetic" patients (initial A1c results of 5.7% and 5.8%) who developed diabetes. A chi-square test indicated a significant difference: 109 out of 4,079 patients in the "normal" group developed diabetes compared to 179 out of 3,680 patients in the "prediabetic" group ($\chi^2(df = 1) = 24.12$, $p < 0.00001$). We then looked at differences in outcomes by grouping patients whose initial A1c results only differed by 0.1%, analogous to the survey design we used in Study 1.

Group 1 compared patients with initial A1c results of 5.5% to patients with initial A1c results of 5.6%. Paralleling the survey results from Study 1, which found no differences in evaluations of 5.5% vs 5.6%, the number of patients who developed diabetes was roughly equivalent: 50 out of 2,037 compared to 59 out of 2,042 ($\chi^2(df = 1) = 0.702$, $p = 0.402$).

Group 2 compared the number of patients with initial A1c results of 5.6% ("normal") who developed diabetes to the number of patients with initial A1c results of 5.7% who developed diabetes ("prediabetic"). Like the survey study results from Study 1, which found perceived risk and anticipated anxiety significantly increased when the 0.1% difference corresponded to a label change, a chi-square test indicated a significant association between the number of patients who developed diabetes and the label given to their initial A1c results: 59 out of 2,042 compared to 80 out of 1,942 ($\chi^2(df = 1) = 4.171$, p = 0.0411).

Group 3 compared the number of patients with initial A1c results of 5.7% ("prediabetic") who developed diabetes to the number of patients with initial A1c results of 5.8% ("prediabetic") who developed diabetes. A chi-square test indicated a significant association between the number of patients who developed diabetes and their initial A1c results: 80 out of 1,942 compared to 99 out of 1,738 ($\chi^2(df = 1) = 7.597$, p = 0.0460). This result is consistent with the results from Study 1, which found that perceived risk and anticipated concern were more sensitive to different A1c results when the results were no longer labeled "normal."

One possible explanation for these results is that A1c values above 5.6% accurately reflect a critical level above which patients are at significantly higher risk of developing diabetes – i.e., that the observed associations are due to the differences in A1c results, not differences in diagnostic labels. If that were the case, we would expect the same pattern of results when comparing patients who received their initial results before the prediabetes label was introduced in 2003. The data we received from Tufts Medical Center included 1,018 A1c test results from 466 patients that were collected before 2003. When we analyzed these data, none of the comparisons between patients whose initial A1c results differed by 0.1% were significant (all p-values > 0.14), suggesting that the psychological differences highlighted by Study 1 are more

than mere coincidence: Study 2 patients whose A1c results initially bordered on "normal" seemed to experience significantly different outcomes depending on whether they were labeled as "normal" or as "prediabetic."

General Discussion

Taken together, the results from Studies 1 and 2 underscore the powerful effects labels have on the ways in which people make sense of A1c test results. None of the foregoing is intended as an argument against diagnostic labels per se. Rather, it is intended to highlight the importance of considering how such labels are applied, the ambiguity labels tend to hide, and the effects they have on both patients and clinicians alike. Simple changes in semantic connotations can have profound effects on psychology and behavior. For example, describing problematic use of drugs and alcohol as "Substance Use Disorder" rather than "Substance Abuse Disorder" significantly affects perceived blame and willingness to treat people struggling to change harmful habits [20], which is why the official diagnosis was renamed in 2013 [21]. Patients receiving emergency care just after their 40th birthday compared to just before are 10% more likely to be screened for and 20% more likely to be diagnosed with Ischemic Heart Disease, reducing the number of missed diagnoses and increasing the probability of receiving lifesaving medical care [22]. Patients who need coronary-artery bypass grafting (CABG) surgery are significantly more likely to receive it if they happen to see their doctor 2 weeks before their 80th birthdays compared to 2 weeks after [23]. Like the patients with A1c results just at the borderline of indicating "prediabetes," these examples illustrate the consequences of thinking categorically and the importance of the language used to distinguish between categories. If the purpose of the "prediabetes" label is to encourage lifestyle changes known to mitigate cardiovascular and diabetic health risks [24] – risks similarly faced by patients whose A1c results are labeled

"normal" but who border on "prediabetes" – this study suggests we may need a more nuanced vocabulary to interpret A1c test results.

Conclusion

The ability to categorize is fundamental to human intelligence and adaptive functioning [25; 26]. Diagnostic labels facilitate effective medical care [27; 28; 29], but like any form of categorization, they tend to obscure the blurriness between categories [30]. Whether the consequences of the borderline effect manifest because patients make distorted inferences [31], doctors use oversimplified heuristics [22; 23], or some combination thereof, these data suggest no difference can make a difference when it leads to categorical thinking that inhibits the ability to appreciate the blurry boundaries between categories.

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