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Individual Pattern Analysis of Cognitive Appraisals Associated with Depressive Symptoms in Youth with Inflammatory Bowel Disease

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Abstract

The stigmatizing nature and negative social sequelae of IBD are potential contributors to youth depressive symptoms. Indeed, two studies in particular [1] [2] found evidence supporting a mediation model in which IBD-stigma was indirectly associated with depressive symptoms through thwarted social belongingness. Although these investigations highlighted the role of stigma and social isolation in youth depressive symptoms, such aggregate-level results present interesting inferential challenges. Namely, despite statistical significance, these studies cannot tell us the number of youth for whom this mediation model actually applied. The present study reanalyzed data from these two samples utilizing person-centered *pattern analysis* methods to test the purported stigma → thwarted belongingness → depressive symptoms mediation model. Participants were 178 youth aged 10 - 18 with a confirmed diagnosis of IBD previously reported in Gamwell *et al.* and Roberts *et al.* Results revealed that although both stigma and thwarted belongingness were associated with depressive symptoms, only about half the participants in both samples could be traced through the mediation model. Findings highlight the *group-to-person generalizability* problem inherent in aggregate-level analyses and the potential misinterpretation of group-level data as representing the majority of respondents in a given study. Results also highlight the advantage of person-centered research methodologies that can advance individual-level insights and enhance the clinical meaningfulness of data. Future studies utilizing person-centered methods could provide medical and behavioral health professionals with guidance for tailoring intervention strategies

to address the individual mental health needs of youth with IBD.

Keywords

Pediatric IBD, Depression, Person-Centered Methods, Observation Oriented Modeling

1. Introduction

Inflammatory bowel disease (IBD) represents a group of disorders in which chronic autoimmune responses cause inflammation of the digestive tract. The clinical presentation of IBD can impair physical and psychosocial functioning due to intrusive and potentially stigmatizing symptoms, including abdominal pain, fatigue, unintentional weight loss, bloody stool, frequent bowel movements, and diarrhea [3]. IBD is fairly common and impacts 1.2 million Americans, with 25% diagnosed during childhood [4]-[6]. Beyond the medical and physical challenges associated with IBD management, youth also experience difficulties with psychological and social adjustment [7]. Indeed, studies indicate that youth with IBD experience higher levels of depressive symptoms compared to their healthy peers and youth with other chronic medical conditions [8] [9]. Clinically elevated depressive symptoms have been observed in 20% - 26% of youth with IBD [10] [11]. Although some studies indicate that IBD clinical disease activity is related to depressive symptoms, others report no association between disease activity and depressive symptoms [12]-[15]. These findings are taken to suggest that factors other than IBD disease activity contribute to depressive symptoms.

Two studies in particular examining the embarrassing nature and negative social sequelae of IBD have identified both illness stigma (*i.e.*, experienced/anticipated social devaluation) and thwarted belongingness (*i.e.*, social isolation/disenfranchisement) as reliable correlates of depressive symptoms in youth with IBD. Gamwell and colleagues [1] found evidence for a mediation path in which illness stigma was associated with increased youths' thwarted social belongingness, which was subsequently associated with elevations in depressive symptoms. A later study by Roberts and colleagues [2] replicated this illness stigma → thwarted belongingness → depressive symptoms mediation model. Thus, for youth with IBD, thwarted belongingness has been theorized to be a result of the stigma associated with embarrassing IBD symptoms (e.g., frequent bathroom use, bloody stool, fecal incontinence) that may lead to feelings of social isolation/disengagement and depressive symptoms. Although these findings point out important psychosocial features of the IBD disease experience related to youth depressive symptoms, the use of aggregate (*i.e.*, group-level) statistics in these studies presents interesting conceptual and inferential challenges.

1.1. Pitfalls and Limitations of Aggregate Statistical Analyses

Aggregate statistics such as means, variances, and correlations are commonly used

to summarize sample-level observations. Such statistics are undeniably useful when attempting to describe observations in the aggregate (*i.e.*, for the group) but are not without controversy or limitations. It is well known, for instance, that the value of a sample mean can be greatly influenced by a small minority of extreme scores which can also produce a skewed distribution of data. Further, aggregate-level statistics are fraught with similar imprecision when examining associations between variables. Anscombe [16] for example demonstrated how data can produce identical bivariate correlations, despite having radically different patterns (*i.e.*, linear; linear with an outlier; nonlinear with an extreme outlier; and curvilinear). Considered alone, group-level correlation statistics can miss important pattern differences like these in the data.

Perhaps more importantly, aggregate statistics may have limited applicability to individual outcomes. For instance, Speelman and McGann [17] created four repeated-measures data sets with mean difference scores equal in magnitude, differing only slightly in their variances across data sets. Aggregate statistical analyses and accompanying significance tests of these data revealed comparable hypothesis-consistent group differences across the four samples. However, inspection of individual difference scores in each sample revealed remarkable variability, with many standing in direct opposition to the hypothesized effect. Similarly, re-analysis of data from previously published studies have shown how group-level conclusions based on aggregate statistics may not match conclusions based on individual patterns of responses [18] [19].

With respect to mediation modeling specifically, Brown and Grice [20] and Grice *et al.* [21] found that aggregate analyses may reveal partial or full mediation effects and explain statistically significant proportions of variance in the outcome variable, but a majority of individuals in the sample may exhibit patterns of responses inconsistent with the model. Thus, although a particular mediation model or analysis may account for significant variance for *participants as a group*, it may not accurately reflect individual behaviors or patterns of behaviors for *participants in the group*. Stated differently, significant results based on traditional aggregate data analysis inform us how participants on average perform in a certain way but cannot inform us of the proportion of participants in a sample for whom a given model actually fits. In practice, when using aggregate-based analysis we lose the individual outcomes but often mistakenly interpret findings as if they represent the majority of individuals in the group under study (*i.e.*, *group-to-person generalizability problem*; [19]).

1.2. Person-Centered Analysis

Given these limitations, there is increased interest in person-centered methods of data conceptualization and analysis that permit researchers and practitioners to overcome the group-to-person generalizability problem [17]-[19] [22]. These methods are not rooted in traditional aggregate statistics but are instead based on the raw observations (*i.e.*, data) themselves and analyzed in such a way as to draw

explanatory inferences about individuals rather than groups. Because these methods require researchers to examine patterns of individual responses, they overcome the pitfalls and limitations of aggregate statistics like those discussed above.

More specifically, with person-centered methods like the various pattern analysis techniques in Grice's [23] Observation Oriented Modeling (OOM) software, individuals' responses in the data are examined, and those who fit the predicted theoretical pattern are identified and then tallied. Grice converts this tally to a percentage and refers to it as the *Percent Correct Classifications* (PCC) index, whereas Speelman and McGann [17] refer to it simply as *pervasiveness*. Further, distribution-free randomization tests can be used to compute probability statistics (*c*-values), which can aid in the interpretation of results from person-centered analyses. Low *c*-values (e.g., <0.10) generated from randomization tests indicate that the observed patterns in the data can be plausibly explained by the theoretical model. High *c*-values indicate that the most plausible explanation for the results is physical chance [24]. Unlike traditional *p*-values used in null hypothesis significance testing, these tests are not subject to restrictive and unrealistic assumptions such as homogeneous population variances, normal population distributions, and random sampling.

1.3. The Present Study

In the present study we used person-centered methods to re-analyze data from two pediatric IBD samples. Following the procedures of Brown and Grice [20] and Grice *et al.* [21] we attempted to trace individual youths through the illness stigma → thwarted belongingness → depressive symptoms mediation model reported by Gamwell *et al.* [1] and Roberts *et al.* [2]. Specifically, we analyzed each sample separately using the *Crossed Orderings Pattern Analysis* in the OOM software [25] to determine the number of youths who could be correctly classified by the proposed mediation model. In effect, youths with relatively high scores on the illness stigma and thwarted belongingness measures were expected to have corresponding high scores on the depressive symptoms measure, and youths with relatively low scores on the illness stigma and thwarted belongingness measures were expected to have corresponding low scores on the depressive symptoms measure.

2. Method

2.1. Participants and Procedure

Participants were 178 youth aged 10 - 18 with a confirmed diagnosis of IBD from independent data sets previously reported in Gamwell *et al.* ([1]; N = 80) and Roberts *et al.* ([2]; N = 75). Also, subsequent to the publication of Roberts *et al.*, 25 additional participants were recruited into the study protocol and were included in the present study. Two participants (one from each sample) were excluded due to missing data, resulting in *N*'s for each sample of 79 and 99, respectively. Participants from both studies were recruited during outpatient appointments at a pediatric gastroenterology clinic within a large teaching hospital in the Southwest

United States. Separate protocols for the original studies were conducted in accordance with American Psychological Association ethical guidelines and were approved by the hospital Institutional Review Board.

Data collection for the Gamwell *et al.* sample took place from 2015-2017. The majority of participants were female (41 female, 38 male) and self-identified as white (71%). Participants were diagnosed with either Crohn's disease (N = 50; 63%) or ulcerative colitis (N = 29; 37%) and had an average illness duration of 2.9 years. The vast majority of participants (N = 67; 85%) were rated as having quiescent disease, 8 (10%) as mild, 3 (4%) as moderate, and 1 (1%) as severe. Sixteen participants (20%) were prescribed steroid medication.

Data collection for the Roberts *et al.* sample took place between 2018-2020. The majority of participants were male (43 female, 56 male) and self-identified as white (78%). Participants were diagnosed with either Crohn's disease (N = 50; 51%) or ulcerative colitis (N = 49; 49%) and had an average illness duration of 2.0 years. The majority of participants (N = 58; 59%) were rated as having quiescent disease, 23 (23%) as mild, 15 (15%) as moderate, and 3 (3%) as severe. Twenty-two participants (22%) were prescribed steroid medication.

2.2. Measures

The *Physicians Global Assessment* (PGA) was completed by the pediatric gastroenterologist to provide an estimate of IBD disease activity. The PGA is based on physician clinical impressions of disease factors (e.g., abdominal pain/tenderness, stool characteristics, etc.). It yields an index of clinical disease activity, with higher scores indicating greater IBD activity (*i.e.*, 1 = *quiescent*, 2 = *mild*, 3 = *moderate*, and 4 = *severe*).

The *Stigma Scale-Child* (SS-C) is an 8-item self-report measure of youth experiences of stigma related to IBD. The SS-C is adapted from the Child Stigma Scale [26] to include wording related specifically to IBD (e.g., "How often do you feel people may not like you if they know you have IBD?"). Items on the SS-C are measured on a 5-point Likert scale (1 = "never" to 5 = "very often"). A total score, ranging from 8 to 40, is calculated by summing the items with higher scores indicating greater perceived illness stigma.

The *Interpersonal Needs Questionnaire-Thwarted Belongingness Subscale* (INQ-TB; [27]) is a 9-item self-report measure that assesses feelings of not belongingness to a social group or connecting with others (e.g., "I often feel like an outsider at school or with my friends") INQ-TB items are rated on a 7-point Likert scale (1 = "not at all true for me" to 7 = "very true for me"). Total scores, ranging from 9 to 63, are calculated by summing the items; higher scores indicate increased perceived thwarted belongingness.

The *Children's Depression Inventory-2nd Edition* (CDI-2; [28]) is a youth self-report measure that assesses the presence of depressive symptoms over the past two weeks. Each of the 28 items is scored on a Likert Scale of 0 to 2 (e.g., 0 = "I am sad once in a while", 1 = "I am sad many times", 2 = "I am sad all the time"), with higher

sum scores (ranging from 0 to 56) indicating more severe depressive symptoms.

2.3. Analysis Plan

For each sample, preliminary analyses were conducted to obtain descriptive statistics for illness stigma (SS-C), thwarted belongingness (INQ-TB), and depressive symptoms (CDI-2), and to describe how these variables were dichotomized. Although mediation models are ideally tested using the original scaling of the variables, the wide and varied ranges of scale values and markedly skewed distributions in the present data made this approach impractical. Following Brown and Grice [20] and Grice *et al.* [21], each variable was consequently dichotomized using a median split to create high and low groups.

The primary analyses were conducted in two steps using a *Crossed Orderings Pattern Analysis* in the latest version of the Observation Oriented Modeling (OOM; [25]) software. Pairwise relationships between the three variables were first examined. The proposed mediation model (illness stigma → thwarted belongingness → depressive symptoms) was then tested. The principal statistic of interest was the Percent Correct Classifications (PCC) index, which indicates the percentage of children correctly classified by each analysis. A PCC value of 50% was furthermore considered the baseline level of classification, as a clinically meaningful result should correctly classify more than half of the children in the sample. A randomization test with 5000 iterations was also performed for each analysis to generate a chance value (*c*-value). A low *c*-value (e.g., ≤0.10) indicates that the observed pattern summarized by the PCC is unlikely to have arisen by chance alone, thereby supporting a causal inference [24].

3. Results

3.1. Sample 1: Gamwell *et al.* ([1]; N = 79)

3.1.1. Preliminary Analyses

Descriptive statistics for the present sample revealed positively skewed distributions for the illness stigma (SS-C; $z_{skew} = 3.01$, $M = 17.66$, $Mdn = 16.00$, $SD = 7.65$), thwarted belongingness (INQ-TB; $z_{skew} = 3.12$, $M = 18.42$, $Mdn = 15.00$, $SD = 8.54$), and depressive symptom measures (CDI-2; $z_{skew} = 3.10$, $M = 8.71$, $Mdn = 7.00$, $SD = 6.63$). The three variables were dichotomized using their respective median values. The SS-C scores ranging from 8 to 15 were classified as "low stigma" and those with scores from 16 to 40 were classified as "high stigma". The INQ-TB scores from 9 to 15 were classified as "low thwarted belongingness" and those ranging from 16 to 63 were classified as "high thwarted belongingness". The depressive symptom scores were reordered such that scores from 0 to 7 on the CDI-2 were classified as "low depression" and those from 8 to 56 were classified as "high depression".

3.1.2. Primary Analyses

Pairwise pattern analyses. Initial pairwise pattern analyses were conducted to

examine the relation between stigma (SS-C) and depressive symptoms (CDI-2), and between thwarted belongingness (INQ-TB) and CDI-2 depressive symptoms. Results revealed that 58 of 79 youth in the sample were correctly classified by corresponding high-low scores on the SS-C and CDI-2 measures (PCC = 73.42%). Pairwise pattern analysis also indicated that 57 youth in the sample were accurately classified by corresponding high-low scores on the INQ-TB and CDI-2 measures (PCC = 72.15%). Randomization tests yielded *c*-values of <0.001 for both analyses, suggesting that the PCC's for the SS-C → CDI-2 and INQ-TB → CDI-2 patterns of observations were not likely the result of physical chance.

Mediation pattern analyses. Pattern analysis for Segment 1 of the mediation model (SS-C → INQ-TB) revealed that 54 of the 79 youth responded in a way consistent with predictions (*i.e.*, corresponding high-low scores on the SS-C and INQ-TB), resulting in a Percent Correct Classifications (PCC) index of 68.35% (*c*-value = 0.002). Of the 54 youth accurately classified in Segment 1, 45 were correctly classified in Segment 2 of the mediation model (INQ-TB → CDI-2; PCC = 83.33%, *c*-value ≤ 0.001). Thus, 45 of 79 youths in the sample could be accurately traced through the proposed mediation model (PCC = 56.96%, *c*-value < 0.001), and this pattern of observations was not likely the result of physical chance. As can be seen in Figure 1, results for the full SS-C→ INQ-TB → CDI-2 model show that 21 youth were correctly classified as having relatively high scores on all three variables, whereas 24 youth were correctly classified as having relatively low scores on all three variables.

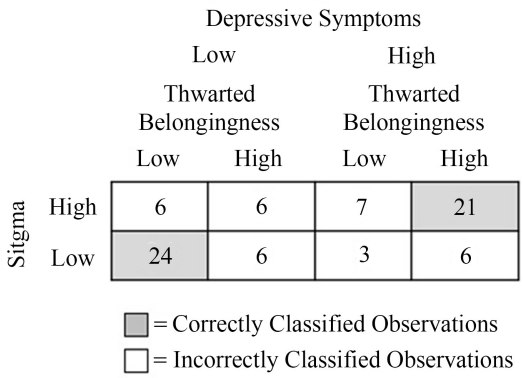

Figure 1. Sample 1 pattern analysis of the stigma→thwarted belongingness→depressive symptoms model.

With person-centered analyses it is often instructive to examine particular individuals at the top and bottom ends of the distribution of the outcome variable in a mediation model. Six youth (8%) scored ≥ 20 on the CDI-2 depressive symptom inventory. Of these, only two failed to be classified correctly. One youth reported relatively low stigma (SS-C = 11) despite reporting the highest level of depressive symptoms (CDI-2 = 27) in the sample, while another youth reported relatively low thwarted belongingness (INQ-TB = 21) despite reporting relatively high depressive symptoms (CDI-2 = 12). By contrast, six youth (8%) scored zero

on the CDI-2 scale. Of these, only one was classified incorrectly due to reporting a relatively high level of thwarted belongingness (INQ-TB = 22). Seventy-five percent of the youth at the extreme ends of the depression scale distribution could therefore be successfully traced through the mediation model.

3.2. Sample 2: Roberts *et al.* ([2]; N = 99)

3.2.1. Preliminary Analyses

Descriptive statistics revealed positively skewed distributions for the illness stigma (SS-C, z_{skew} = 3.25, M = 15.42, Mdn = 14.00, SD = 6.12), thwarted belongingness (INQ-TB, z_{skew} = 3.92, M = 20.44, Mdn = 18.00, SD = 10.62), and depressive symptom measures (CDI-2, z_{skew} = 5.37, M = 8.81, Mdn = 7.00, SD = 6.97). The three variables were again dichotomized using their respective median values. The SS-C was reordered such that "low stigma" was associated with scores ranging from 8 to 13, and those with scores from 14 to 40 were classified as "high stigma." The INQ-TB was reordered such that scores from 9 to 17 were classified as "low thwarted belongingness" and those with scores ranging from 18 to 63 were classified as "high thwarted belongingness". The ordering for CDI-2 remained the same as in Sample 1 (low depression = 0 to 7, high depression = 8 to 56).

3.2.2. Primary Analyses

Pairwise pattern analyses. Pairwise pattern analysis of the relation between stigma (SS-C) and depressive symptoms (CDI-2) revealed that 62 of 99 youth in the sample were correctly classified by corresponding high-low scores on the SS-C and CDI-2 measures (PCC = 62.63%). Pattern analysis also indicated that 77 of 99 youth were correctly classified by corresponding high-low scores on the thwarted belongingness (INQ-TB) and depressive symptoms (CDI-2) measures (PCC = 77.78%). Randomization tests yielded low c-values for the SS-C → CDI-2 and INQ-TB → CDI-2 analyses indicating the PCCs for both patterns of observations were not likely the result of physical chance (0.01 and <0.001, respectively).

Mediation pattern analyses. Segment 1 analysis of the mediation model revealed that a little more than half of participant responses (60 out of 99) were consistent with the SS-C → INQ-TB prediction (PCC = 60.61, c-value = 0.03). Of the 60 youth who were accurately classified in Segment 1, 50 were correctly classified by corresponding high-low scores in Segment 2 of the pattern analysis (INQ-TB → CDI-2; PCC = 83.33%, c-value < 0.001). Thus, 50 of the total 99 participants were correctly classified in the SS-C → INQ-TB → CDI-2 mediation model (PCC = 50.51%). The c-value (<0.001) suggests that the pattern of observations for the total model was not likely the result of physical chance. As shown in Figure 2, 24 youth were correctly classified as having high scores on all three variables, whereas 26 youth were correctly classified as having low scores on all three variables.

With respect to examining particular youth with the highest and lowest scores on the outcome variable, eight youth (8%) in this sample scored ≥20 on the CDI-2 depressive symptom inventory. Of these, only one failed to be classified cor-

rectly. One youth reported a relatively low stigma score (SS-C = 13) despite reporting a high level of depressive symptoms (CDI-2 = 22). By contrast, six youth (6%) scored zero on the CDI-2. Of these youth, two were classified incorrectly due to reporting relatively high levels of stigma (SS-C values of 15 and 17). Thus, seventy-nine percent of these fourteen youth at the extreme ends of the depression scale distribution could be successfully traced through the mediation model.

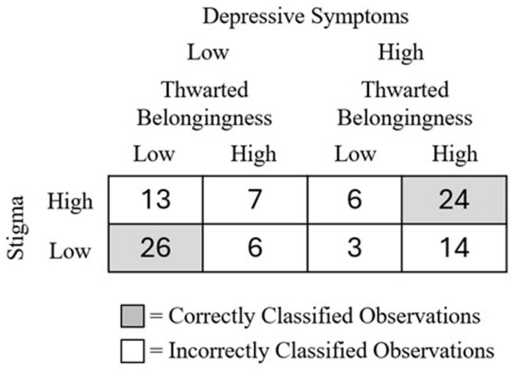

Figure 2. Sample 2 pattern analysis of the stigma→thwarted belongingness→depressive symptoms model.

4. Discussion

Two pediatric IBD studies have identified key cognitive appraisal variables (*illness stigma* and *thwarted belongingness*) associated with youth depressive symptoms and found evidence for an indirect path in which heightened IBD-related stigma is linked to feelings of social isolation, which is then linked to an increased vulnerability for depressive symptoms (*i.e.*, illness stigma → thwarted belongingness → depressive symptoms; [1] [2]). Although these studies point out important psychosocial features of the IBD disease experience related to depressive symptoms, the use of aggregate statistics creates interesting inferential challenges—most notably the inability to inform us of the proportion of youth in these studies who actually fit the mediation model.

In the present study we utilized Observation Oriented Modeling [23] to reanalyze the data from these two previously published studies to provide an individual-level inspection of the number of youths who could be successfully traced through the illness stigma → thwarted belongingness → depressive symptoms mediation model observed in each of these samples. Based on this mediation model, we sought to classify participants who endorsed corresponding high and low levels of IBD-related stigma and thwarted belongingness, and of those, the number of participants who reported corresponding high and low levels of stigma, thwarted belongingness, and depressive symptoms.

Pattern analysis results indicated that a majority of youth in the Gamwell *et al.* [1] sample demonstrated response patterns in which high and low stigma scores corresponded with high and low thwarted belongingness scores, but only slightly more than half had corresponding stigma, thwarted belongingness, and depres-

sive symptoms scores. In other words, just over half the participants in the total sample could be correctly classified by the illness stigma → thwarted belongingness → depressive symptoms mediation model. Similar results were obtained for the Roberts *et al.* [2] sample, in that a small majority of youth had corresponding high and low stigma and thwarted belongingness scores, but only half the participants in the sample could be accurately traced through the hypothesized mediation model. Thus, the illness stigma → thwarted belongingness → depressive symptoms mediation model reported in both studies was *statistically significant* using aggregate-level statistics. However, individual-level pattern analysis results in the present study indicated that essentially half of the youth in both samples actually fit this model.

Foremost, the present results should be interpreted as a cautionary note regarding both the broader group-to-person generalizability problem inherent in translating aggregate-level analyses to individual-level processes, and by illustration, the accuracy of the illness stigma → thwarted belongingness → depressive symptoms mediation model as a putative sequence for depression in youth with IBD. The primary concern related to individual-level inferences about youth adjustment based on group-level analyses comes from evidence highlighting the tendency on the part of professionals and research psychologists to interpret aggregate-level empirical results as representing a meaningful majority of individuals in a sample and, by extension, the population [19]. Numerous studies demonstrate that statistically significant findings do not guarantee that even a small majority of participants in a given sample actually demonstrate patterns of behaviors (*i.e.*, responses) consistent with theoretical expectation (e.g., [18] [22] [29]). In fact, the present results suggest that even when youth report exceedingly high levels of depression, health professionals cannot assume that the purported illness stigma → thwarted belongingness → depressive symptoms pathway is at work. Thus, for medical and behavioral health professionals working with youth experiencing depression, this tendency to draw individual-level conclusions from aggregate data can potentially result in overgeneralization of and/or over-reliance on group-level findings to inform clinical interventions for adjustment difficulties at the expense of exploring other potential avenues that could guide more individualized treatment strategies for youth with IBD and their families.

To be clear, our results urge caution in generalizing group-level findings to individual-level processes, but they should not be taken as evidence that illness stigma and thwarted belongingness are unrelated to depressive symptoms in this population. For example, an examination of the pairwise analyses indicate fairly sizeable proportions of youth for whom stigma and thwarted belongingness corresponded with depressive symptoms scores. In other words, from our data a reasonable interpretation could suggest that stigma is related to depressive symptoms in 60% - 70% of youth, and thwarted belongingness is related to depressive symptoms in roughly 75% of youth. Moreover, a small majority of youth across both samples (60% - 70%) had corresponding scores on the stigma and thwarted be-

longingness measures. Of this group, the vast majority (83%) also demonstrated corresponding levels of thwarted belongingness and depressive symptoms.

For clinicians these findings could suggest several things. First, for youth who report both stigma and thwarted belongingness (vs. stigma or thwarted belongingness alone), there may be a greater likelihood that feelings of social isolation play a clinically meaningful role in the development and/or maintenance of depressive symptoms. Thus, for this sub-group of youth, cognitive-behavioral interventions would be indicated (*i.e.*, stigma-reduction and behavioral activation strategies) to address negative IBD appraisals, increase social problem-solving, and encourage involvement in rewarding activities (e.g., [2] [9] [30] [31]).

At the same time, however, these same results also identify a sizeable minority of youth for whom something (or somethings) other than the presence/absence of stigma deserve consideration to understand the social marginalization and associated depressive symptoms experienced by youth with IBD. Thus, for youth whose feelings of social isolation are not a function of IBD stigma, clinicians will want to look for other contributing factors. Several risk factors associated with both thwarted belongingness and depressive symptoms have been identified in the literature (e.g., peer victimization, body image disturbance; [32] [33]). The utilization of person-centered methods to identify sub-groups of youth for whom these variables play an important role would provide meaningful clinical information pointing to the need for individual skills-based and group/peer-based intervention strategies (e.g., [34] [35]).

Finally, while speculative, our results could also suggest that youth in our sample who reported scores discordant with the proposed mediation model may possess resilience capabilities (e.g., coping skills, peer/family support, mindfulness) that resulted in lower depressive symptoms, despite elevated stigma and/or thwarted belongingness. Although such resilience variables are understudied in pediatric IBD populations, existing evidence demonstrates their role in circumventing the impact of negative IBD illness experiences on youth adjustment outcomes (e.g., [36]-[38]). Such findings suggest that the exploration of contextual/resilience factors in future studies could provide additional avenues for strengths-based interventions to minimize the impact of IBD on youth emotional well-being (see [39]).

5. Limitations

Several limitations temper the present findings. First, the cohort of participants were selected from a single outpatient specialty clinic in one geographic location, which limits the generalizability of our findings to the larger population of youth with IBD from different geographic and cultural backgrounds. Non-random samples can also adversely impact causal claims drawn from mediation models via the introduction of biases that can distort the relationships between variables. Skewed distributions like those in these two samples might amplify or obscure linear relationships in traditional mediation modeling, making it hard to trust that the model's inferred temporal sequence reflects reality rather than statistical artifacts

[40] [41].

A second limitation of the current study is the use of median splits to dichotomize each of the three variables in the mediation model. The wide and varied scale ranges (9 to 63 for the INQ-TB, 8 to 40 for the SS-C, and 0 to 56 for the CDI-2) and skewed distributions necessitated such binning so individual youth could be traced through the proposed mediation model. Binning is generally frowned upon for reasons related to significance testing (viz., decreased statistical power) and for treating individuals with scores close to the cut points as essentially the same as those with scores close to the variable's extremes [42] [43]. Regarding the second concern it should be noted that, while not reported above, analyses of the mediation model using trichotomized variables yielded substantially lower PCCs (<32%) for the two samples. More generally, it can be argued that binning has its advantages (e.g., see [44]). Restructuring continuous variables into categories can simplify complex data, making it easier to interpret and communicate findings in ways that are useful to medical professionals who often rely on empirically derived and replicated thresholds for decision-making (e.g., blood pressure categories; see [45], for a recent review of such methods). It is therefore noteworthy that the cut-points for the three variables across both IBD samples were nearly identical, supporting their consistency.

A third limitation of the current study entails the temporal ambiguity of mediation models based on correlational and cross-sectional data. Mediation modeling assumes a specific causal sequence, but statistical results alone cannot confirm this direction, leaving the true order ambiguous [46]. Without experimental manipulation or longitudinal data, the analysis might equally support reverse causation, such as the supposed outcome driving the mediator, undermining claims of causality. The original temporal claims derived from aggregate level results reported by Gamwell *et al.* [1] and Roberts *et al.* [2] are subject to this limitation, and the person-centered results in the present study must also be treated as speculative and rest largely upon theoretical explication.

6. Summary

It is clear that youth with IBD experience illness stigma and thwarted belongingness, and that both are associated with depressive symptoms. However, our person-centered (*i.e.*, pattern analysis) results indicate that of the youth with elevated depression scores, only about *half* experience depressive symptoms as a function of thwarted belongingness stemming from illness stigma as suggested in previous studies [1] [2]. Our findings suggest alternative ways in which stigma and thwarted belongingness may be related to depressive symptoms in youth with IBD and, although speculative, how other potential risk and resilience variables may help explain the low concordance of responses observed for the stigma → thwarted belongingness → depressive symptoms mediation model.

In general, these findings also highlight the value of utilizing person-centered research methods that require scientists to engage the data in novel ways to allow

for more robust theory building and describing results in a meaningful way such that providers may develop a wider array of empirically informed intervention strategies [18] [47]. Future studies utilizing person-centered analyses could allow for more accurate observations of individual patterns of risk and resilience variables across individual, familial, and social domains, which may provide medical and behavioral health professionals with clearer guidance for tailoring intervention strategies to address the individual medical management and mental health needs of youth with IBD [48] [49].

Author Statement

All authors have made substantial contributions to all of the following: 1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, 2) drafting the article or revising it critically for important intellectual content, 3) final approval of the version to be submitted.

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Conflicts of Interest

The authors declare no conflicts of interest.

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