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Development of a Brief Parent-Report Screen for Common Gastrointestinal Disorders in Autism Spectrum Disorder

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Abstract

Gastrointestinal dysfunction in children with autism spectrum disorder (ASD) is common and associated with problem behaviors. This study describes the development of a brief, parent-report screen that relies minimally upon the child's ability to report or localize pain for identifying children with ASD at risk for one of three common gastrointestinal disorders (functional constipation, functional diarrhea, and gastroesophageal reflux disease). In a clinical sample of children with ASD, this 17-item screen identified children having one or more of these disorders with a sensitivity of 84%, specificity of 43%, and a positive predictive value of 67%. If found to be valid in an independent sample of children with ASD, the screen will be useful in both clinical practice and research.

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Compliance with Ethical Standards

Potential conflicts of interest: All authors declare no conflicts of interest

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

Keywords

autism; screen; gastrointestinal; GI; comorbidities; behavior

Introduction

Evidence is growing that gastrointestinal dysfunction is highly prevalent in children with ASD(McElhanon, McCracken et al. 2014), is associated with problem behaviors(Maenner, Arneson et al. 2012, Mannion, Leader et al. 2013, Mazefsky, Schreiber et al. 2014, Mannion and Leader 2016, Marler, Ferguson et al. 2017) and has potential neurobiological significance(Margolis, Li et al. 2016, Margolis 2017). However, clinicians and researchers lack a brief parent-report screen to help them identify children with autism spectrum disorder (ASD) who likely have a gastrointestinal disorder (GID). To be useful, such a screen must take into account the fact that children with ASD, regardless of spoken language level, may not communicate or localize pain in typical ways due to their social communication and sensory processing impairments(Oberlander and Zeltzer 2014).

This report describes the development of a brief parent-report screen for common, often painful GIDs in children with ASD. The screen is derived from a longer parent-report questionnaire developed by pediatric gastroenterologists participating in the Autism Speaks - Autism Treatment Network (AS-ATN). The original ATN questionnaire was designed to assess signs and symptoms of three common GIDs---functional constipation, functional diarrhea and gastroesophageal reflux disease (GERD)--- selected by gastroenterologists as common and impairing in children with ASD(2005). The original ATN questionnaire was novel in three respects: it predominantly assessed GI signs (observable manifestations) rather than symptoms (subjective experiences); it included manifestations of GERD; and it asked about specific subtle recurring motor acts (e.g. arching back, stiffening or squeezing the buttocks, applying pressure to the abdomen, or gagging during meals) observed by pediatric gastroenterologists in children with ASD presenting with GID(Buie, Campbell et al. 2010). To date, several studies have reported significant correlations between selected items in the ATN questionnaire and problematic behaviors in children with ASD(Mannion, Leader et al. 2013, Mazurek, Vasa et al. 2013, Mazefsky, Schreiber et al. 2014, Mannion and Leader 2016).

This report is the first to describe the derivation from items in the original ATN questionnaire of a screening measure for functional constipation, functional diarrhea, and GERD in children with ASD. It is based upon a two-stage study conducted at two of the ATN registry sites. In the first stage, caretakers completed the ATN questionnaire. In the second stage, pediatric gastroenterologists, unaware of parental questionnaire responses, evaluated each child for the clinical diagnosis of functional constipation, functional diarrhea and/or GERD. Using data from both stages, this study identifies a smaller set of maximally predictive items as a screen for these three common GIDs in children with ASD.

METHODS

This study was approved by the Institutional Review Boards of The Massachusetts General Hospital and Columbia University Medical Center. Legal guardians signed consent forms for all participants. Children and adolescents signed assent forms when appropriate.

Recruitment

Potential participants were all ATN Registry enrollees coming sequentially to the two ATN sites for clinical care during defined time intervals (at MGH between 09/05/2008 and 07/16/2010 and at CUMC between 05/08/09–04/26/2010). All ATN enrollees met the criteria shown in E-Table 1. The study was described to parents as having two stages, the first being completion of a questionnaire by the parent and the second being a free consultation with a pediatric gastroenterologist who would be unaware of parental responses on the questionnaire. Of all the AS-ATN Registry enrollees coming to the two sites for clinical care during these defined time intervals, parents of 131/229 (57.2%) consented to their child's participation and completed the pediatric gastroenterology consultation. (see E-Table 2).

Procedures and Forms

Stage 1: Parent Questionnaire—The 35-item Gastrointestinal Symptom Inventory (ATN GI Symptom Inventory(2005)), was the basis for screen development. An additional 42 follow-up items were asked only if the parent endorsed certain of the core 35 items; these 42 items were not included in screen development. From the core 35 items, nine items were removed: one of these was gender-specific (menstruation in girls), two asked about a GI condition (e.g. constipation), not about signs or symptoms, four asked parents to make comparisons about bowel movements involving "as usual" without being anchored to specific frequencies, one item asked about weight gain or loss and one item asked the parent to make a global assessment of their confidence level in assessing the child's pain. The remaining 26 core items assessing GI signs and symptoms were included in screen development. For these 26 items, the time frame for 23 items was "in the last three months" for 23 items, for one "in the last year" for two, "ever". Two of the 26 items assessed bowel movement frequency and consistency, respectively, and offered five parental response options, including "unsure". The remaining 24 items offered three parental response options: "yes" "no" or "unsure". The "unsure option" was included to allow for parental uncertainty based on the child's self-report or lack of opportunity to observe, as might occur when a child toilets independently. Importantly, only 5 of the 26 items referenced subjective experiences (symptoms); these included pain (three items), nausea (one item), and bloating. The other 21 items are observable manifestations (signs) of GI problems.

Stage 2: Expert Clinical Diagnosis—For each child seen in consultation, the gastroenterologist (……) recorded his/her impression about the presence or absence of functional constipation, functional diarrhea, and/or GERD using published criteria adapted by the authors for children with ASD (Table 1). Recommendations for follow-up (for any reason) were recorded and shared with the family. After completion of any follow-up and a chart review, the consulting gastroenterologist reached a final impression as to the presence/

absence in each participant of functional constipation, functional diarrhea, and/or GERD. Additionally, each GID was categorized as (1) previously recognized but unresolved despite ongoing treatment at the time of the study consultation visit or (2) newly recognized as a result of the study consultation.

Examination of Non-participants, Site and Examiner Differences—Those ATN enrollees whose parents declined participation in the study did not differ from those whose parents agreed with respect to gender, age, race, ethnicity or spoken language level. Parents of nonparticipants, however, were less likely to have a college degree (see E-Table 2). As there were no significant site differences among participants in child and family characteristics (with the exception of more Hispanic families at the CU site) and no site or study doctor differences in GID rates (data not shown), the combined sample was used for all analyses. Two of the 131 children who participated in the GI consultation were missing data on the parent questionnaire. Thus, these two cases are only included in the description of the diagnosed GI conditions and are not included in the development of the screen.

Analyses

Initially, the frequency distribution of parent responses to the 26 core items were compared. The rate of "unsure" response for GI signs are compared to rates of "unsure" responses to GI symptoms. Rates of "unsure" were also compared across age, gender and whether the child was verbal. The remaining analyses were conducted in four stages:

1. Exploratory factor analysis to identify separate dimensions within the core 26 items in the ATN questionnaire. At this stage, we also compared the means of the scales based on these dimensions for children with and without each of the three clinician-diagnosed GIDs using t-tests;
2. Estimation of two-parameter Item Response Theory (IRT) models(Embretson and Reise 2000) to identify items that were highly discriminatory for these dimensions. The extent to which these items can predict GIDs was subsequently assessed;
3. Subjecting the remaining scale items to ROC analyses to determine the optimal cut point for identifying additional cases of GID; and
4. Combining the results of stages 2 and 3 to develop screening algorithms for each of the three GIDs, as well as a screen for having any one of the three GIDs. The sensitivity, specificity, and positive predictive value (PPV) of each algorithm is reported.

The rationale for beginning with factor analysis was to obtain sets of internally consistent items to subject to ROC analysis. In ROC analysis, however, items are examined as equivalent contributors to the dimension. Thus the IRT analysis was conducted to find items that may be particularly useful for identifying cases of GID.

Missing data on individual items in the parent questionnaire was rare. Scales were constructed under the assumption that missing data on a particular item represented a "no" response.

RESULTS

Sample Description

Table 2 shows the demographic characteristics of the sample; 43.4% were non-verbal. GIDs were highly prevalent. Of the 131 children in the sample, 76 had at least one GID diagnosed at the study consultation, most commonly functional constipation (35.1%), followed by GERD (29.8%) and functional diarrhea (5.3%). Twenty-seven children (20.6%), had ≥1 newly recognized GID. Children with at least one GID did not differ significantly from those without a GID on any demographic variables or in terms of spoken language level (E-Table 3). There also were no significant differences between newly and previously recognized GID cases on these variables (E-Table 4).

Item Response Frequency Distribution

As seen in Table 3, readily observable GI signs including motoric acts, had very low rates of "unsure" responses, while parents were much more likely to be unsure about their child's subjective experiences (symptoms) such as pain, nausea, or bloating. The rates of "unsure" responses, however, did not vary by age, gender or level of spoken language (E-Table 5). Subsequent analyses collapse "no" and "unsure" responses.

Factor Analysis

An exploratory factor analysis was conducted on 26 items from the original ATN questionnaire. This resulted in four distinct factors making substantial independent contribution to explained variance in the items (based on the scree plot): a) "Retentive", b) "Expulsive", c) "Gassy", and d) "Motoric" (factor loadings are provided in E-Table 6). Table 4 displays the items belonging to each factor. Items with similar sized loadings on multiple factors were included in both scales created to represent those dimensions. Items in Table 4 that are not in bold are those removed because their inclusion reduced the internal reliability (Cronbach's alpha) of the summed scale.

Relation between Scales and GID

Table 5 compares means scores on the four scales across children with and without a GID. Functional constipation is strongly associated with the Retentive scale and has weaker associations with the Motoric and Gassy scales. GERD is strongly associated with the Motoric scale; it is less strongly and non-significantly related to the Gassy and Expulsive scales. The diagnosis of functional diarrhea has a strong relation with the Expulsive scale, but falls short of statistical significance, likely because of its low prevalence. Functional diarrhea is unrelated to any of the other scales. Finally, the Retentive scale and the Motoric scale are both significantly associated with the likelihood of having any one of the three GID.

Item Analysis

Two-parameter IRT models were estimated for each of the four scales. Figure 1 displays the item characteristic curves for all of the items in each of the scales as well as the item discriminations. The highly discriminatory items in each scale were selected for special

attention in predicting the three clinical GID. These items were not selected based on a fixed discrimination value but rather discrimination (steepness of the item characteristic curve) relative to other items in the scale.

Functional Constipation—Four items on the Retentive scale are distinguished by their steep item characteristic curves relative to the remaining items (Figure 1a): having two or fewer bowel movements (BMs) per week (last 3 months), having pain with BMs (last 3 months), missing activities because of problems with BMs, and missing activities due to pain or discomfort. These four-items were included in a stepwise logistic regression predicting functional constipation (see E-Table 7a). Although the associations of functional constipation with the Gassy and Motoric scales are modest, the highly discriminatory items from these scales were also included in the logistic regression. Even with very loose significance criteria ($p < .10$ for increased F), only two items made an independent contribution to predicting functional constipation: 2 or fewer BMs per week, and missing activities because of problems with BMs. When endorsement of either of these two items is classified as a positive screen, the result is high specificity (89.7%) and excellent PPV (65.2%) (Table 6). The sensitivity, however, is very poor (34.1%). Use of this screen would thus miss nearly two-thirds of subjects with functional constipation.

In an effort to enhance sensitivity, the remaining items in the Retentive scale were subjected to an ROC analysis. This analysis excluded cases already screened positive in the previous step. The results (see E-Table 7b) indicated that the optimal cut-point for identifying additional cases of functional constipation is one or more items. This suggests that the optimal overall screen is endorsement of one or more of any of the six items in the Retentive scale. When this is used as the definition for a positive screen for functional constipation, the sensitivity rises to 75.6%, with a specificity of 61.0% and a PPV of 51.5% (Table 6).

Functional Diarrhea—Functional diarrhea is associated only with the Expulsive scale. The three items in this scale distinguished by high discrimination values (missed activities due to vomiting, spit up 2 or more times in a day, and experienced wretching), however, are not usually considered signs of functional diarrhea. These orally expulsive items, when co-occurring with the other items in the scale suggest a transient infection. An ROC analysis was conducted using the remaining items from the Expulsive scale. These included nausea, need to rush to the bathroom for a BM, Black/tarry BM, missed activities due to problems with BMs, BMs soft/mushy/watery, and a motor act (tilted head to the side and arched back). The results of this analysis (E-Table 8) reveal an optimal cut-point of one or more of these items for identifying cases of functional diarrhea. A screen based on this definition has a sensitivity of 83.3% (5 of 6 cases). The specificity is 51.2% and the PPV is 7.8% (Table 6).

GERD—A diagnosis of GERD is significantly associated with scores on the Motoric scale. It also has non-significant, weak associations with the Expulsive and Gassy scales. The items with comparatively high discrimination values in any one of these three scales were included in a stepwise logistic regression predicting the presence of a diagnosis of GERD (see E-Table 9a for the items included in the regression). After the most strongly associated item (choke, gag, cough or wet sounds during or after swallowing or with meals) entered the model, none of the other items had a significant independent relationship with GERD.

Interestingly, this single item alone captured 40.5% of all cases of GERD (specificity 87.6%; PPV 57.7%) (Table 6). Nonetheless, we considered the rest of the Motoric, Gassy, and Expulsive scales as a means of improving sensitivity. As the Motoric scale is related to functional constipation as well as to GERD, we removed the items explicitly referencing bowel movements and included the remaining Motoric items (tilted head to side and arched back, pushed abdomen, refused foods eaten in the past, stopping all activities 2 + hours due to pain) in an ROC analysis (E-Table 9b), with those already screened positive using the choke/gag item excluded. The ROC indicates an optimal cut-point of two or more of the remaining Motoric scale items.

The remaining screen negatives were then subjected to further ROC analyses involving the Gassy and Expulsive scales. The former was uninformative – the area under the curve (AUC) was less than 0.5. Since the Expulsive scale is related to functional diarrhea as well as to GERD, we conducted a ROC on the oral expulsive items that remain after those in the screen for functional diarrhea were removed. Thus, the ROC was conducted using nausea, spitting up two or more times a day, retching, and missing activities due to vomiting. The optimal cut-point is the endorsement of one or more of these items (E-Table 9b). When the criteria from the ROC analyses for both the motoric items (two or more positive) and the oral expulsive items (one or more positive) were included as a path to a positive screen, the sensitivity rises to 73.0% with a specificity of 64.0% and a PPV or 45.8 (see Table 6).

Any GID—If a positive screen for the presence of any of the three GIDs is defined as one or more positive screens for the individual GID, the result is a highly sensitive screen (83.6%) with a specificity of 43.4% and a PPV of 67.0% (see Table 6). Because a number of items are shared in common by the screens for the individual GIDs, only 17 of the original 26 items are required to screen for the presence of any GID. This instrument is presented here as the ATN-GI Signs and Symptoms Inventory-17 (ATN-GISSI-17) (see Appendix).

It should also be noted that, because of co-occurrence across the three conditions, the overall screen is actually more sensitive for individual conditions than are the component screens (functional constipation sensitivity=84.4%; functional diarrhea sensitivity=100% and GERD sensitivity=86.5%;).

Additional analyses were conducted to see if a yet more parsimonious screen could be used to identify the likely presence of any GID, so that the specific diagnosis could later be determined by a gastroenterologist. A stepwise regression of all highly discriminatory items assessed for the individual screens identified three items that were independently predictive of the presence of a GID -- two or fewer BMs a week, spitting up more than twice per day, and missed activities due to excessive gas (see e-Table 10). A screen defined by endorsement of any one of these three items results in a sensitivity of 38.6%, a specificity of 86.5%, and a PPV of 79.4% (Table 6). While the high PPV means that any individual child referred for a GI consultation on the basis of these screening items has a high probability of having a GID, this screen would miss far too many GIDs to be useful. Thus, the screening algorithm based on the ATN-GISSI-17 is clearly recommended assuming that it can be validated in other ASD samples.

DISCUSSION

This paper aimed to develop a brief parent-report screen for identifying children with ASD likely to benefit from further GI evaluation. This 17-item screen (the AS-ATN GI Signs and Symptoms Inventory-17), derived from a longer questionnaire, targets three common and often painful GIDs—functional constipation, functional diarrhea, and GERD. The screens for the individual disorders are modestly sensitive and specific. The combination of the three screens, however, is quite sensitive as a screen for any of the three GID and is not overly burdensome in terms of false positives (Sens=83.6%; Spec=43.4%; PPV=67.0%).

As expected, given the social communication and sensory processing impairments of children with ASD, rates of parental "unsure" responses were higher for the few items assessing symptoms (subjective experiences of GIDs) than for signs (observable manifestations of GIDs) and did not differ by age or spoken language level. Items involving motoric acts had the lowest rates of parental "unsure" responses and proved particularly useful for identifying cases of GERD, The item "choke, gag, cough, or sound wet during or after swallowing or with meals" identified 40.5% of cases with GERD with high specificity (89.7%), while other motor acts ("tilting his/her head to the side and arched back, push abdomen with his/her hands or your hand, push his/her abdomen against or lean forward against furniture", and "refused foods that would eat in the past") were helpful in increasing the sensitivity of the screen for GERD. The movements of "tilting head/arching back" are referred to by gastroenterologists as "Sandifer's syndrome", which is considered a clinical sign for GERD(Vandenplas, Rudolph et al. 2009). Hopefully, this study will widen awareness of these GERD-associated motoric acts among autism providers who might otherwise limit their differential and further evaluation to possible tics(Simonoff, Pickles et al. 2008) or seizures(Bauman 2010, Jeste and Tuchman 2015, Hung 2016). The importance of GERD in children with ASD is underscored by fact that, in this clinical sample, GERD was nearly as common (29.8%) as functional constipation (35.9 %) and, of the two, had a higher rate (43.6% vs 28.2%) of being newly recognized as a result of the GI consultation.

This study differs from the only other study to compare parent report and clinician diagnoses of GIDs in children with ASD with respect to the parent report instrument(Gorrindo, Williams et al. 2012). That study examined how a general population measure of GI symptoms (the 71-item Questionnaire on Pediatric Gastrointestinal Symptoms (QPGS)-Rome III)(Whitehead, Palsson et al. 2006, Lewis, Palsson et al. 2016)) aligned with gastroenterologists' diagnoses of GIDs in a clinical sample of children with ASD(Gorrindo, Williams et al. 2012). Consistent with this study, they found that parent report identified the presence of any GID better than specific GIDs and also found a high prevalence of gastroenterologist-diagnosed GERD (20%). The AS-ATN-GISSI-17 has the advantage of being a shorter measure that is more suitable for screening and does not include many items about GI symptoms that are typically difficult to ascertain in ASD. The AS-ATN-GISSI-17 also contains items assessing motoric acts that are not included in the QPGS-Rome III.

The AS-ATN-GISSI-17 is now ready for a test of its validity in an independent clinical sample of children with ASD. If found to be valid, it could be used in research to narrow the pool of children with ASD in whom an actual diagnosis (by a gastroenterologist) needs to be

made before inclusion in a study, reducing the time and cost of recruiting and characterizing samples of children with ASD defined by GID status. It could also be useful in clinical care. It is noteworthy that slightly over one fifth of this clinical sample were found to have one or more GID(s) that had not been previously identified. This is particularly concerning because the stereotype that children with ASD have "a high threshold for pain" is not supported by evidence(Oberlander and Zeltzer 2014). Routine screening for common, often painful GIDs in children with ASD is feasible with this brief parent-report instrument. Moreover, while problematic behaviors (e.g., irritability, aggression, self-injury, sleep problems) may occur with a wide range of medical conditions, a screen such as this could allow autism providers to quickly and systematically consider GIDs as a possibility and refer appropriately.

Limitations of the Study

A number of limitations need to be noted. The first pertains to the limited number of cases. This is particularly true for functional diarrhea; the small number of cases may be due to the age of onset criterion (<3 years), which is based on evidence that chronic diarrhea onset after age 3 is usually organic in origin(Guiraldes and Roessler 2013). The small number of cases, together with the overlap between functional diarrhea and GERD in the data, resulted in the identification of a factor (expulsivity) that included items representative of both functional diarrhea and GERD. For example, the description of "tilted his/her head and arched back", usually indicative of Sandifer's syndrome and therefore associated with GERD, was also associated with functional diarrhea. Despite this limitation, we chose to include diarrhea as one of our screened conditions because several studies have reported a high incidence of diarrhea in children with ASD (Kang, Wagner et al. 2014, McElhanon, McCracken et al. 2014, Alabaf, Gillberg et al. 2018, Holingue, Newill et al. 2018). Further, we wanted to emphasize the possibility that previous reports of high rates of parent-reported signs and symptoms suggestive of diarrhea(McElhanon, McCracken et al. 2014) are in fact encopresis-that is, frequent, loose stools around a large, hard stool mass due to functional constipation, which often co-occurs with GERD(Baran, Cagan Appak et al. 2017). A GI consultation may be necessary to distinguish between encopresis and functional diarrhea(Colombo, Wassom et al. 2015). Further research employing different and larger samples will determine whether this low prevalence for functional diarrhea is unique to our sample.

A possible second limitation arises from the nature of the item analysis. The IRT analysis identified items that might be especially effective in distinguishing the presence or absence of GI conditions, rather than treating all items the same as in a ROC analysis. A different sample might have produced a different set of items for the screen, though it is likely that the resulting sensitivity and specificity would be similar. It also should be acknowledged that there was occasional missing data on the parent questionnaire and this that this may have resulted in negative screen results that would have been positive under under the circumstance of complete data.

Finally, it should be noted that the analyses here were undertaken for the purpose of developing a screen. This screen will have to be tested on other ASD samples before full confidence can be placed in its validity. It should be noted, however, that the screen for "any GID" returned values for sensitivity, specificity, and PPV that were virtually identical for the

two study sites. The two sites were quite different in terms of ethnic composition, providing reason to hope that the screen can be effectively applied across clinical care settings.

While adding new questions not included in the original ATN questionnaire might identify some of the 16.4% of children with a GID condition who were missed. Such increases in sensitivity are likely to come at the expense of specificity and positive predictive value (PPV). Full sensitivity can be achieved by eschewing use of a screen and referring all children with ASD for a GI consultation. In order for a screen for GID to be worth the time and effort involved in its administration in a clinical or research setting, it must achieve a substantial reduction in false positives over the alternative of universal referral to a pediatric gastroenterologist. While it is true that a third of the children with positive screens in this sample did not ultimately have one of the three GIDs, this rate of over-referral seems an acceptable burden in light of the fact that it correctly identified over 80% of the sample who had at least one GID.

It is important to note that since the completion of this study, new Rome criteria (Rome IV) have been developed that include the diagnoses of functional diarrhea and functional constipation. Although use of the Rome IV criteria would have been optimal for use in this study, questions asked of all study participants were based on the wording noted in the Rome III criteria. As such, it was not possible to reanalyze the data based on even the small differences in definitions for which the study participants were not provided. The differences between Rome III and Rome IV, however, are minor with regards to the diagnostic criteria for functional constipation and functional diarrhea(Simren, Palsson et al. 2017). The major differences between rome III and Rome IV include the addition of four new diagnoses that we did not screen for. These diagnoses, however, would have been highly unlikely to be diagnosed in our pediatric population (opioid-induced constipation, narcotic bowel syndrome/opioid-induced GI hyperalgesia and cannabinoid hyperemesis syndrome) or very challenging to diagnose given a requirement of the ability to verbalize and localize pain (reflux hypersensitivity)(Simren, Palsson et al. 2017, Yamasaki and Fass 2017). The screen results would thus not likely differ(Simren, Palsson et al. 2017).

Common and often painful childhood GIDs may go unrecognized in children with ASD due to their communication and sensory processing impairments. The brief parent-report screen developed here is now ready for a validation study in an independent clinical sample of children with ASD. Once validated, it is hoped that its use will improve clinical care and facilitate research.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

(2005). Autism Treatment Network, GI symptom inventory questionnaire, vers. 3.0. New York, NY, Autism Speaks.

Alabaf S, Gillberg C, Lundstrom S, Lichtenstein P, Kerekes N, Rastam M and Anckarsater H (2018). "Physical health in children with neurodevelopmental disorders." J Autism Dev Disord.

Baran M, Cagan Appak Y, Karakoyun M, Yalcinkaya S, Eliacik K and Dundar BN (2017). "The overlap of gastroesophageal reflux disease and functional constipation in children: the efficacy of constipation treatment." Eur J Gastroenterol Hepatol 29(11): 1264–1268. [PubMed: 28914696]

Bauman ML (2010). "Medical comorbidities in autism: challenges to diagnosis and treatment." Neurotherapeutics 7(3): 320–327. [PubMed: 20643385]

Buie T, Campbell DB, Fuchs GJ 3rd, Furuta GT, Levy J, Vandewater J, Whitaker AH, Atkins D, Bauman ML, Beaudet AL, Carr EG, Gershon MD, Hyman SL, Jirapinyo P, Jyonouchi H, Kooros K, Kushak R, Levitt P, Levy SE, Lewis JD, Murray KF, Natowicz MR, Sabra A, Wershil BK, Weston SC, Zeltzer L and Winter H (2010). "Evaluation, diagnosis, and treatment of gastrointestinal disorders in individuals with ASDs: a consensus report." Pediatrics 125 Suppl 1: S1–18. [PubMed: 20048083]

Colombo JM, Wassom MC and Rosen JM (2015). "Constipation and Encopresis in Childhood." Pediatr Rev 36(9): 392–401; quiz 402. [PubMed: 26330473]

Embretson SE and Reise SP (2000). Item response theory for psychologists. Maheah, New Jersey: Lawrence Erlbaum Associates, Publishers.

Gorrindo P, Williams KC, Lee EB, Walker LS, McGrew SG and Levitt P (2012). "Gastrointestinal dysfunction in autism: parental report, clinical evaluation, and associated factors." Autism Res 5(2): 101–108. [PubMed: 22511450]

Guiraldes E and Roessler JL (2013). Functional Diarrhea in Toddlers (Chronic Nonspecific Diarrhea) Pediatric Neurogastroenterology, Springer: 355–358.

Holingue C, Newill C, Lee LC, Pasricha PJ and Daniele Fallin M (2018). "Gastrointestinal symptoms in autism spectrum disorder: A review of the literature on ascertainment and prevalence." Autism Res 11(1): 24–36. [PubMed: 28856868]

Hung K (2016). "Epilepsy Comorbidity of Autism in Children." Epilepsy J 2: e011.

Jeste SS and Tuchman R (2015). "Autism Spectrum Disorder and Epilepsy: Two Sides of the Same Coin?" J Child Neurol 30(14): 1963–1971. [PubMed: 26374786]

Kang V, Wagner GC and Ming X (2014). "Gastrointestinal dysfunction in children with autism spectrum disorders." Autism Res 7(4): 501–506. [PubMed: 24753336]

Lewis ML, Palsson OS, Whitehead WE and van Tilburg MAL (2016). "Prevalence of Functional Gastrointestinal Disorders in Children and Adolescents." J Pediatr 177: 39–43 e33. [PubMed: 27156185]

Maenner MJ, Arneson CL, Levy SE, Kirby RS, Nicholas JS and Durkin MS (2012). "Brief report: Association between behavioral features and gastrointestinal problems among children with autism spectrum disorder." Journal of autism and developmental disorders 42(7): 1520–1525. [PubMed: 22012246]

Mannion A and Leader G (2016). "An investigation of comorbid psychological disorders, sleep problems, gastrointestinal symptoms and epilepsy in children and adolescents with autism spectrum disorder: A two year follow-up." Research in Autism Spectrum Disorders 22: 20–33.

Mannion A, Leader G and Healy O (2013). "An investigation of comorbid psychological disorders, sleep problems, gastrointestinal symptoms and epilepsy in children and adolescents with autism spectrum disorder." Research in Autism Spectrum Disorders 7(1): 35–42.

Margolis KG (2017). "A role for the serotonin reuptake transporter in the brain and intestinal features of autism spectrum disorders and developmental antidepressant exposure." J Chem Neuroanat 83–84: 36–40.

Margolis KG, Li Z, Stevanovic K, Saurman V, Israelyan N, Anderson GM, Snyder I, Veenstra-VanderWeele J, Blakely RD and Gershon MD (2016). "Serotonin transporter variant drives preventable gastrointestinal abnormalities in development and function." J Clin Invest 126(6): 2221–2235. [PubMed: 27111230]

Marler S, Ferguson BJ, Lee EB, Peters B, Williams KC, McDonnell E, Macklin EA, Levitt P, Margolis KG and Beversdorf DQ (2017). "Association of Rigid-Compulsive Behavior with Functional Constipation in Autism Spectrum Disorder." Journal of Autism and Developmental Disorders 47(6): 1673–1681. [PubMed: 28289979]

Mazefsky CA, Schreiber DR, Olino TM and Minshew NJ (2014). "The association between emotional and behavioral problems and gastrointestinal symptoms among children with high-functioning autism." Autism 18(5): 493–501. [PubMed: 24104507]

Mazurek MO, Vasa RA, Kalb LG, Kanne SM, Rosenberg D, Keefer A, Murray DS, Freedman B and Lowery LA (2013). "Anxiety, sensory over-responsivity, and gastrointestinal problems in children with autism spectrum disorders." Journal of abnormal child psychology 41(1): 165–176. [PubMed: 22850932]

McElhanon BO, McCracken C, Karpen S and Sharp WG (2014). "Gastrointestinal symptoms in autism spectrum disorder: a meta-analysis." Pediatrics 133(5): 872–883. [PubMed: 24777214]

McElhanon BO, McCracken C, Karpen S and Sharp WG (2014). "Gastrointestinal symptoms in autism spectrum disorder: a meta-analysis." Pediatrics 133(5): 872–883. [PubMed: 24777214]

Oberlander TF and Zeltzer LK (2014). Pain in Children with Autism Mental Health and Pain, Springer: 191–209.

Simonoff E, Pickles A, Charman T, Chandler S, Loucas T and Baird G (2008). "Psychiatric disorders in children with autism spectrum disorders: prevalence, comorbidity, and associated factors in a population-derived sample." J Am Acad Child Adolesc Psychiatry 47(8): 921–929. [PubMed: 18645422]

Simren M, Palsson OS and Whitehead WE (2017). "Update on Rome IV Criteria for Colorectal Disorders: Implications for Clinical Practice." Curr Gastroenterol Rep 19(4): 15. [PubMed: 28374308]

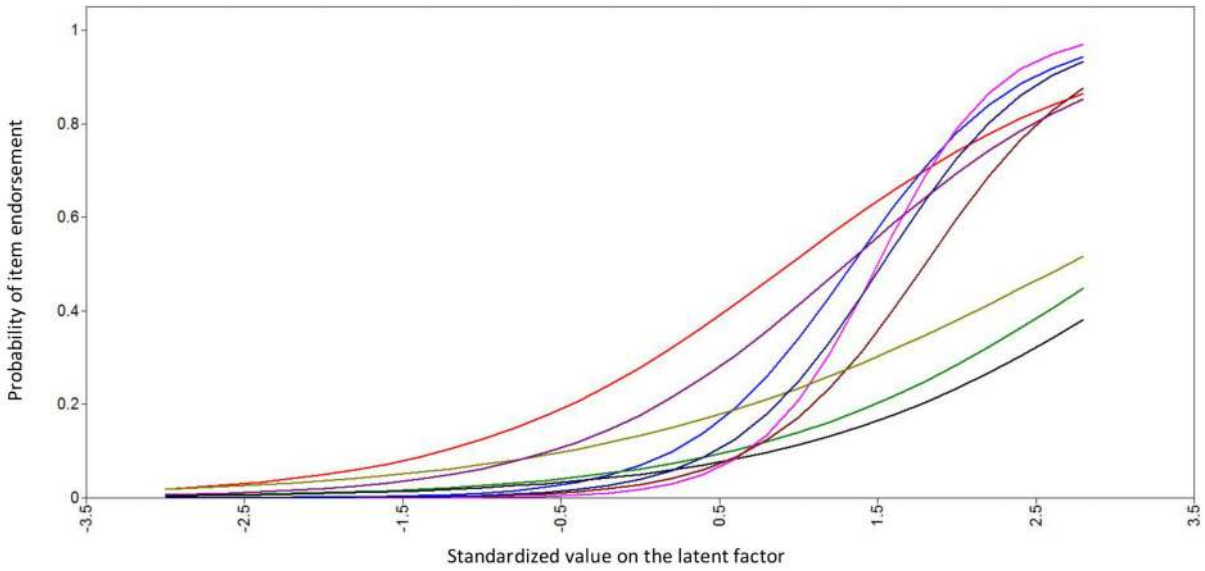
Vandenplas Y, Rudolph CD, Di Lorenzo C, Hassall E, Liptak G, Mazur L, Sondheimer J, Staiano A, Thomson M, Veereman-Wauters G, Wenzl TG, North H American Society for Pediatric Gastroenterology, Nutrition, H. European Society for Pediatric Gastroenterology and Nutrition (2009). "Pediatric gastroesophageal reflux clinical practice guidelines: joint recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN)." J Pediatr Gastroenterol Nutr 49(4): 498–547. [PubMed: 19745761]

Whitehead W, Palsson O, Thiwan S, Talley N, Chey W, Irvine E, Drossman D, Thompson W and Walker L (2006). "Development and validation of the Rome III diagnostic questionnaire" Rome III: The Functional Gastrointestinal Disorders. 3rd Edition ed. McLean, VA: Degnon Associates, Inc: 835–853.

Yamasaki T and Fass R (2017). "Reflux Hypersensitivity: A New Functional Esophageal Disorder." J Neurogastroenterol Motil 23(4): 495–503. [PubMed: 28992673]

a. Retentive Scale

Item Characteristic Curves



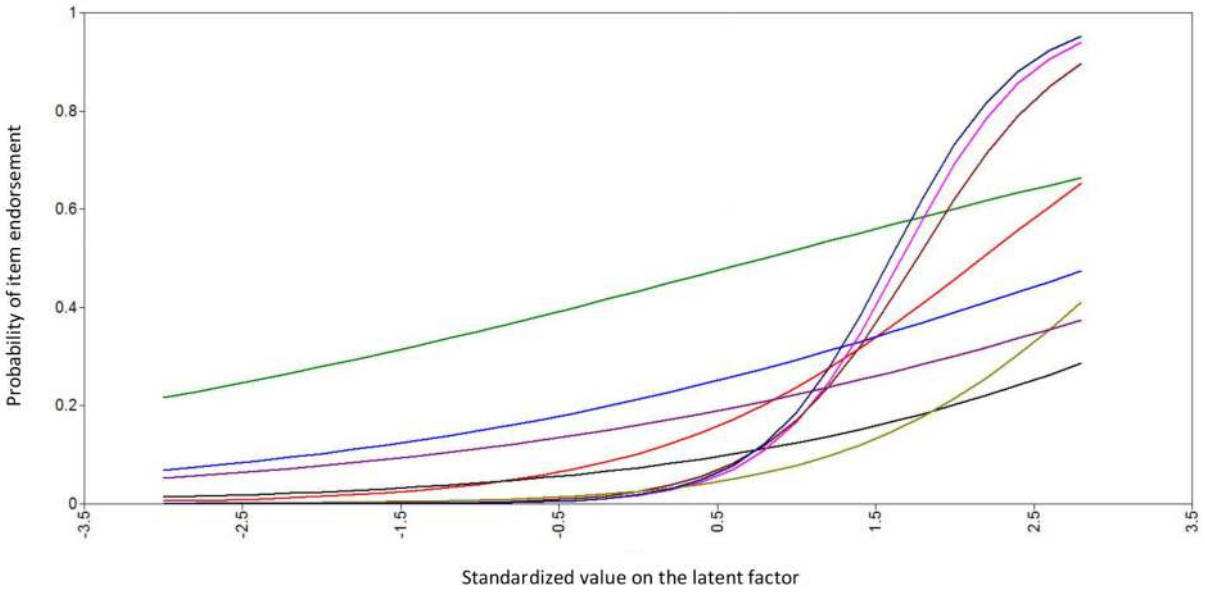
Item Discriminations

Line Color	Item	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value
	Miss activities due to pain/discomfort	2.656	1.191	2.230	0.026
	BMs ≤ 2 times per week	2.078	0.893	2.328	0.020
	Miss activities due to problems w/ BMs	1.963	0.832	2.360	0.018
	Appear to feel pain when having a BM	1.929	0.885	2.179	0.029
	BMs hard or very hard	1.176	0.494	2.380	0.017
	Abdominal/belly pain	1.000	0.000	undef	1.000
	Ever had red blood in/after a BM*	0.893	0.467	1.913	0.056
	Regurgitation	0.871	0.456	1.908	0.056
	Punch chest or neck, put fist into mouth, or bite hands or wrist	0.693	0.348	1.993	0.046

*Items with an asterisk ask whether the GI sign/symptom has ever occurred. All other items refer only to the last 3 months.

b. Expulsive Scale

Item Characteristic Curves



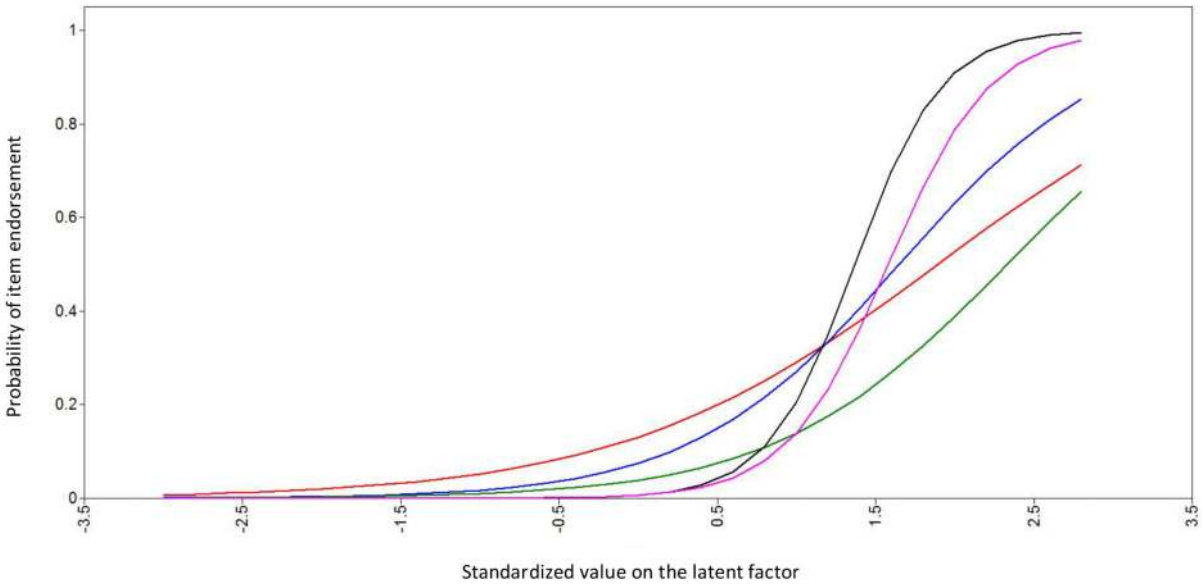
Item Discriminations

Line Color	Item	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value
	Missed activities due to vomiting	2.478	1.433	1.729	0.084
	Spit up 2 or more times per day	2.425	1.230	1.971	0.049
	Experienced retching	2.076	0.945	2.197	0.028
	Tilted head to the side and arched back	1.168	0.684	1.708	0.088
	Nausea	1.000	0.000	undef	1.000
	Ever had a black, tarry BM*	0.576	0.518	1.113	0.266
	Rush to the bathroom for a BM	0.430	0.427	1.007	0.314
	BMs very soft or mushy or watery	0.408	0.398	1.023	0.306
	Stain/soil underwear	0.339	0.398	0.852	0.394

*Items with an asterisk ask whether the GI sign/symptom has ever occurred. All other items refer only to the last 3 months.

c. Gassy Scale

Item Characteristic Curves



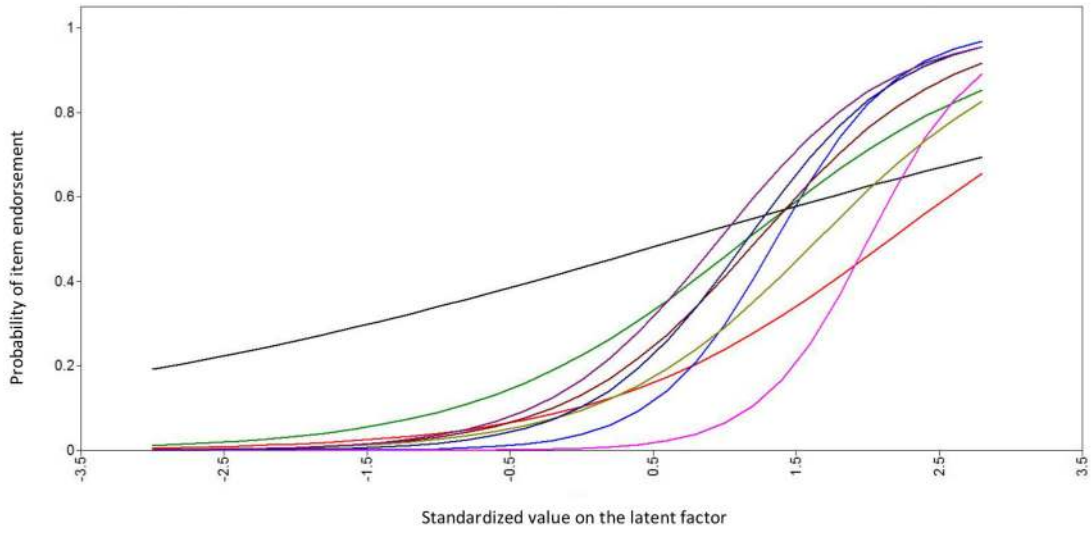
Item Discriminations

Line Color	Item	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value
	Miss activities due to pain and/or discomfort	3.656	1.960	1.866	0.062
	Miss activities due to excessive gas	3.133	1.538	2.037	0.042
	Severe GI pain lasting ≥ 2 hours causing child to stop all activities*	1.523	0.546	2.789	0.005
	Trouble gaining weight	1.374	0.621	2.212	0.027
	Experienced Bloating	1.000	0.000	undf	------

*Items with an asterisk ask whether the GI sign/symptom has ever occurred. All other items refer only to the last 3 months.

d. Motoric Scale

Item Characteristic Curves



Item Discriminations

Line Color	Item	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value
	Tilted head to the side and arched back	2.649	1.114	2.378	0.017
	Pass mucus/phlegm during a BM	2.369	0.718	3.297	0.001
	Choke, gag, cough/sound wet during/after swallowing or with meals	1.864	0.726	2.566	0.010
	Started to refuse many foods that he/she would in the past	1.666	0.536	3.110	0.002
	Push abdomen with hands or push against/lean forward over furniture	1.524	0.511	2.981	0.003
	Punch chest/neck, put fist into mouth or bite hands/wrist	1.355	0.484	2.801	0.005
	Stiffen legs/squeeze bottom and legs together when need to have a BM	1.067	0.416	2.566	0.010
	Severe GI pain lasting ≥ 2 hours causing child to stop all activities*	1.000	0.000	undf	-------
	Stain/soil underwear	0.390	0.260	1.496	0.135

*Items with an asterisk as whether the GI sign/symptom has ever occurred. All other items refer only to the last 3 months.

Fig. 1.

Item Characteristic Curves and Discriminations for the Four ATN GI Symptoms Inventory Dimensions

Table 1:

Study Definitional Criteria for Active GI Conditions

Regurgitation/Gastroesophageal Reflux (r/GER): ***must include all of the following:***	
☐	Persistent or recurrent pain or discomfort centered in the upper abdomen (above the umbilicus), such as tapping chest*
☐	Pain not relieved by defecation or associated with the onset of a change in stool frequency or form
☐	No evidence of an inflammatory, anatomic, metabolic or neoplastic process * Criteria fulfilled at least once per week for at least 2 months prior to diagnosis
Constipation: ***must include 2 or more of the following in a child with a developmental age of at least 4 years with insufficient criteria for diagnosis of IBS***	
☐	Two or fewer defecations in the toilet per week*
☐	At least one episode of fecal incontinence per week*
☐	History of retentive posturing or excessive volitional stool retention
☐	History of painful or hard bowel movements
☐	Presence of a large fecal mass in the rectum
☐	History of large diameter stools which may obstruct the toilet * Criteria fulfilled at least once per week for at least 2 months prior to diagnosis
Diarrhea: ***must include all of the following:***	
☐	Daily painless, recurrent passage of three or more large, unformed stools
☐	Symptoms that last more than 4 weeks
☐	Onset of symptoms that begins between 6 and 36 months of age
☐	Passage of stools that occurs during waking hours
☐	Normal growth if caloric intake is adequate
Food Allergy (FA): must be confirmed by:	
☐	Positive RAST

Table 2:

Characteristics of the Study Sample (N = 131)

Gender (% male)	82.4
Age at Evaluation Mean (± SD)	7.8 (3.8)
Race (% Minority)	25.2
Ethnicity (% Hispanic or Latino)	13.0
Primary Parent Education (% < post-grad)[a]	69.4
ADOS Module (% Module 1)	43.4
IQ (Mean ± SD)[b]	71.0(20.4)

[a]Ten cases were missing primary parent education level (8 from MGH, 2 from CUMC; 8 with ≥1 active GI conditions, 2 with no active GI conditions)

[b]Two cases were missing IQ data (both from MGH, and both with ≥1 active GI conditions).

Table 3.

Original 43 Items: Distribution of Responses and Correlations of Positive Responses with Active GI Conditions as Determined by Pediatric Gastroenterologists

Item #		Total N	Yes %	Unsure %	Any GI	G	C	D	F
	GI Symptoms								
B1a	In the last 3 months, has your child experienced abdominal (belly) pain?	125	32.8	22.4	**0.32****	**0.33*****	**0.31****	0.03	0.12
B1b	In the last 3 months, has your child experienced nausea?	120	13.3	20.0	0.09	0.00	−0.03	0.15	0.06
B1c	In the last 3 months, has your child experienced bloating?	126	16.7	23.0	0.16	0.14	**0.27****	−0.14	0.19
B1d	In the last 3 months, has your child experienced not being hungry after eating very little?	82	30.5	3.7	0.11	0.06	0.10	**0.29****	0.12
B1e	**Parent-Defined GI Conditions**								
oth const	In the last 3 months, has your child experienced constipation?	109	22.9	6.4	0.19	0.15	**0.30****	0.07	0.02
oth diarr	In the last 3 months, has your child experienced diarrhea?	107	21.5	6.5	0.11	**0.23***	0.05	0.19	**0.20***
oth refvo	In the last 3 months, has your child experienced vomiting/reflux?	127	7.9	7.1	0.18	**0.22***	−0.01	0.06	0.00
othoth	In the last 3 months, has your child experienced other GI or tummy symptom(s)?	107	22.4	14.0	0.13	−0.10	−0.02	−0.06	0.11
	GI Signs: Gated Questions								
B2	If yes to any of one of B1a- B1e, in the last 3 months:								
B2a	Did the symptom(s) get better after having a BM?	77	51.9	27.3	0.12	0.04	0.22	−0.08	0.05
B2b	Were your child's BMs softer or more watery than usual?	92	30.4	9.8	0.14	0.21	−0.08	0.19	0.11
B2c	Were your child's BMs harder or lumpier than usual?	90	24.4	13.3	0.13	0.08	**0.38*****	−0.18	−0.08
B2d	Did your child have more BMs than usual?	91	17.6	7.7	0.16	0.08	−0.02	−0.12	0.16
B2e	Did your child have fewer BMs than usual?	91	18.7	7.7	0.09	−0.08	**0.44*****	−0.14	−0.16
B2f	Did your child's symptom(s) occur before eating or when hungry?	75	17.3	36.0	0.22	0.21	0.14	0.04	0.15
B2g	Did the symptom(s) change after your child ate?	76	23.7	31.6	−0.02	**0.29***	−0.13	−0.10	0.14
B2h	Did the symptom(s) wake your child from sleep?	77	15.6	22.1	0.18	0.09	0.03	−0.13	0.00
	GI Signs: Non-Gated Questions								
B7	In the last 3 months, how often did your child usually have a BM?								
B7a	≤2 times per week	125	12.8	4.8	0.12	−0.15	**0.32*****	0.02	−0.12
B7b	3 times a week up to and including 3 times a day	125	80.0	4.8	N/A	N/A	N/A	N/A	N/A
B7c	> 3 times a day	125	2.4	4.8	0.09	0.13	−0.01	−0.04	**0.20***
B8	In the last 3 months, what were your child's BMs usually like?								

Item #		Total N	Yes %	Unsure %	Any GI	G	C	D	F
B8a	Hard or very hard	122	24.6	11.5	0.08	−0.06	**0.28****	−0.06	−0.05
B8b	Not too hard and not too soft	122	45.9	11.5	N/A	N/A	N/A	N/A	N/A
B8c	Very soft or mushy or watery	122	18.0	11.5	0.09	0.05	−0.08	0.18	**0.19***
B9	In the last 3 months, did your child appear to feel pain when having a BM?	125	16.8	22.4	**0.22***	0.09	**0.32*****	−0.03	0.00
B10	In the last 3 months, did your child have to rush to the bathroom for a BM?	118	24.6	18.6	0.12	0.13	−0.01	0.05	0.16
B11	In the last 3 months, did your child pass mucus or phlegm during a BM?	123	14.6	22.8	0.17	−0.02	0.12	−0.11	**0.23***
B12	In the last 3 months, did you see your child stiffen his/her legs or squeeze his/her buttocks (bottom) and legs together when he/she felt the need to have a BM?	124	28.2	18.5	**0.20***	0.07	0.17	0.03	0.13
B13	After passing a stool, was your child:								
B13a	More active?	80[a]	31.3	27.5	**0.27***	0.01	**0.28***	0.03	0.14
B13b	Less irritable?	79[a]	40.5	24.1	**0.37****	0.13	**0.38****	−0.14	0.16
B14	In the last 3 months, did your child stain or soil underwear?	119	47.9	5.0	0.11	0.05	**0.20***	−0.05	0.01
B17a	In the last 3 months, has your child spit up 2 or more times a day?	125	9.6	1.6	0.13	0.16	0.04	0.18	0.01
B17b	In the last 3 months, has your child experienced retching?	123	9.8	0.8	0.13	−0.03	**0.21***	−0.08	0.01
B17c	In the last 3 months, has your child tilted his/her head to the side and arched back?	123	4.9	9.8	0.06	0.11	−0.10	0.12	0.15
B17d	In the last 3 months, has your child regurgitated food and chewed it again?	122	7.4	2.5	0.10	0.10	−0.01	0.10	0.09
B18	In the last 3 months, has your child had trouble gaining weight?	125	8.0	10.4	−0.01	0.00	−0.03	−0.06	0.06
	Activity Restriction								
B19	In the last 3 months, did your child miss activities because of:	126	11.1	2.4					
B19a	Pain and/or discomfort?	126	10.3	0.0	0.10	0.04	**0.18***	0.04	−0.08
B19b	Vomiting?	124	9.7	2.4	0.02	0.06	0.03	0.05	−0.12
B19c	Problems with BMs?	125	8.8	4.0	**0.20***	0.09	**0.22***	−0.08	0.07
B19d	Excessive gas?	126	11.1	2.4	0.07	0.16	0.09	0.06	0.04
	Behaviors								
B21	In the last 3 months, did your child push his abdomen with his/her hands or your hands, push his/her abdomen against or lean forward over furniture?	126	21.4	8.7	**0.24****	0.16	**0.20***	−0.12	0.08
B22	In the last 3 months, did your child punch her/his chest or neck, put her/his fist into their mouth, or bite her/his hands or wrist without a reason?	125	16.0	4.0	0.18	**0.19***	0.13	0.00	0.11
B23	In the last 3 months, did your child choke, gag, cough, or sound wet during or after swallowing or with meals?	126	20.6	3.2	**0.27****	**0.31*****	0.07	0.07	**0.25****

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Item #		Total N	Yes %	Unsure %	Any GI	G	C	D	F
B24	In the last 3 months, has your child started to refuse many foods that he or she would eat in the past?	125	26.4	4.0	0.12	**0.20***	0.03	0.03	0.16
	In the last year/ever								
B6	In the last year, did your child have severe GI (tummy pain) that lasted ≥2 hours and caused your child to stop all activities?	117	15.4	17.1	0.08	**0.24***	0.13	0.01	−0.08
B15	Has your child ever had a black, tarry BM?	118	9.3	20.3	0.09	**0.26***	0.08	−0.07	0.06
B16	Has your child ever had red blood in or after a BM?	123	8.9	15.4	0.14	**0.20***	**0.28****	0.07	0.03

Table 4:

Prevalence of Specific Active GI Conditions: None, Any, Isolated, and Comorbid (N = 131)

	N	(% of 131)
No Conditions	49	37.4
Isolated Conditions	50	38.2
Constipation	25	19.1
Diarrhea	3	2.3
Regurgitation/gastroesophageal reflux (r/GER)	16	12.2
Food allergies (RAST+)	6	4.6
Combinations of Two	28	21.4
Constipation + Diarrhea	0	0.0
Constipation + r/GER	8	6.1
Constipation + Food allergies (RAST+)	9	6.9
Diarrhea + r/GER	4	3.0
Diarrhea + Food allergies (RAST+)	0	0.0
r/GER + Food allergies (RAST+)	7	5.3
Combinations of Three	4	3.0
Constipation + Diarrhea + r/GER	0	0.0
Constipation + Diarrhea + Food allergies (RAST+)	0	0.0
Constipation + r/GER + Food allergies (RAST+)	4	3.0
Diarrhea + r/GER + Food allergies (RAST+)	0	0.0
Combinations of Four	0	0.0
Total with Any Condition	82	62.6
Any Constipation	46	35.1
Any Diarrhea	7	5.3
Any r/GER	39	29.8
Any Food allergies (RAST+)	26	19.8

Table 5.

Differences in ATN-GI Signs and Symptoms Inventory-26 Scale Scores across GID

A. Scale: Any GI Condition (number of items: 11, α=0.681, standardized α= 0.661)

Variable label	**Item**	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
gisxb1a1	Last 3 months - Abdominal (belly) pain?	.506	.347	.623
othconst	Parent-defined constipation	.393	.348	.648
othdiarr	Parent-defined diarrhea	.380	.315	.651
othrefvo	Parent defined other reflux or vomiting	.128	.256	.687
gisxb9	Last 3 months - pain with BM?	.346	.217	.657
gisxb12	Last 3 months - stiffen or squeeze buttocks?	.342	.215	.659
gisxb19c	Last 3 months - Miss activitites: Problems with BMs?	.193	.147	.679
gisxb21	Last 3 months - Push abdomen?	.336	.215	.659
gisxb22	Last 3 months - Punching chest or neck, putting fist in mouth, biting hands, wrist?	.324	.220	.661
gisxb23	Last 3 months - Choke, gag, sound wet during/after swallowing or with meals?	.422	.326	.643
gisxb16	Ever Red blood in/after BM?	.149	.150	.683

B. Scale: R/GER (number of items: 11, α = 0.681, standardized α=0.597)

Variable label	**Item**	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
gisxb1a1	Last 3 months - Abdominal (belly) pain?	.480	.418	.529
othdiarr	Parent-defined diarrhea	.116	.228	.622
othrefvo	Parent defined other reflux or vomiting	.223	.421	.594
gisxb2g	Last 3 months - SXs change after eating?	−.093	.078	.656
gisxb21	Last 3 months - Push abdomen?	.366	.306	.562
gisxb22	Last 3 months - Punching chest or neck, putting fist in mouth, biting hands, wrist?	.183	.258	.602
gisxb23	Last 3 months - Choke, gag, sound wet during/after swallowing or with meals?	.579	.499	.513
gisxb24	Last 3 months - Refusing foods that ate in the past?	.291	.276	.580
gisxb6	Last year - severe GI pain >=2hrs caused child to stop activities?	.501	.409	.530
gisxb15	Ever Black, tarry BM?	.186	.250	.600
gisxb16	Ever Red blood in/after BM?	.155	.122	.605

C. Scale: Constipation (number of items: 12, α= 0.769, standardized α= 0.762)

Variable label	**Item**	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
gisxb1a1	Last 3 months - Abdominal (belly) pain?	.218	.532	.777

othconst	Parent-defined constipation	.262	.380	.766
gisxb2a	Last 3 months - Better after having a BM?	.605	.622	.727
gisxb2c	Last 3 months - BMs harder, lumpier than ususal?	.552	.657	.735
gisxb2e	Last 3 months - Fewer BMs than usual?	.622	.715	.728
gisxb7a	In last 3 mos, child had fewer BMs than normal	.478	.680	.745
gisxb8a	In last 3 mos, child's BMs too hard	.331	.531	.762
gisxb9	Last 3 months - pain with BM?	.513	.758	.741
gisxb13b	After BM, less irritable?	.516	.551	.739
gisxb17b	Last 3 months - Retching?	.096	.329	.782
gisxb19a	Last 3 months - Miss activitites: Pain and/or discomfort?	.385	.638	.756
gisxb16	Ever Red blood in/after BM?	.274	.385	.766

D. Scale: Diarrhea (number of items: 3, α= 0.436, standardized α= 0.424)

Variable label	**Item**	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
gisxb1d1	Last 3 months - Not hungry after eating very little	.164	.214	.550
othdiarr	Parent-defined diarrhea	.158	.273	.495
gisxb2b	Last 3 months - BMs softer, more watery than usual?	.541	.335	−.331[a]

E. Scale: FA/RAST+ (number of items: 10, α= 0.677, standardized α= 0.663)

Variable label	**Item**	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
gisxb1c1	Last 3 months - Bloating	.269	.271	.668
othdiarr	Parent-defined diarrhea	.452	.283	.628
gisxb2b	Last 3 months - BMs softer, more watery than usual?	.604	.539	.589
gisxb2d	Last 3 months - More BMs than ususal?	.460	.520	.628
gisxb7c	In last 3 mos, child had more BMs than normal	.316	.189	.666
gisxb8c	In last 3 mos, child's BMs too soft or watery	.481	.459	.622
gisxb11	Last 3 months - Mucus, phlegm during BM?	.369	.239	.647
gisxb19d	Last 3 months - Miss activitites: Excessive Gas?	.197	.304	.675
gisxb22	Last 3 months - Punching chest or neck, putting fist in mouth, biting hands, wrist?	.162	.178	.687
gisxb16	Ever Red blood in/after BM?	.058	.142	.694

Table 6:

Sensitivity (Sens), Specificity (Spec), Positive Predictive Value (PPV), and Negative Predictive Value (NPV) for Scales comprised of items correlating with Any GI Condition and with each of four specific clinical conditions (r/GER, Constipation, Diarrhea, and Food Allergy / RAST+) as assigned by the study GI specialists using 3 different cutpoints

Scale (number of items) / Cutpoints	Sens %	Spec %	PPV %	NPV %
r/GER (11)				
0 vs. 1 or more	89.5	38.2	38.2	89.5
0–1 vs. 2 or more	68.4	64.0	44.8	82.6
0,1,2 vs. 3 or more	50.0	75.3	46.3	77.9
Constipation (16)				
0 vs. 1 or more	91.1	34.1	43.2	87.5
0–1 vs. 2 or more	80.0	54.9	49.3	83.3
0,1,2 vs. 3 or more	71.1	70.7	57.1	81.7
Persistent Diarrhea (3)				
0 vs. 1 or more	100.0	62.5	11.8	100.0
0–1 vs. 2 or more	66.7	82.5	16.0	98.0
0,1,2 vs. 3 or more	0.0	99.2	0.0	95.2
Food Allergy-RAST+ (10)				
0 vs. 1 or more	70.8	47.6	23.9	87.5
0–1 vs. 2 or more	54.2	71.8	31.0	87.1
0,1,2 vs. 3 or more	45.8	85.4	42.3	87.1
Any GI Condition (11)				
0 vs. 1 or more	84.8	58.3	77.0	70.0
0–1 vs. 2 or more	67.1	72.9	80.3	57.4
0,1,2 vs. 3 or more	44.3	87.5	85.4	48.8