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Pediatric Patients with Dyspepsia Have Chronic Symptoms, Anxiety, and Lower Quality of Life as Adolescents and Adults

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Abstract

Background & Aims—Little is known about long-term health outcomes of children with dyspeptic symptoms. We studied the natural history of pediatric patients with dyspeptic symptoms, with and without histologic reflux, compared to healthy controls.

Methods—We performed a prospective study of consecutive new patients, ages 8–16 years, who underwent evaluation for dyspepsia, including upper endoscopy. Patients were assigned to groups with histologic evidence of reflux esophagitis (n=50), or normal histology results (n=53). Healthy children were followed as controls (n=143). Patients and controls were evaluated 5–15 years later. They provided self reports on severity of dyspeptic symptoms, use of acid suppression, quality of life, anxiety, and depression.

Results—When the study began, the groups with histologic evidence for esophagitis and normal histologies did not differ in severity of dyspeptic symptoms, functional disability, or depression. After a mean 7.6-year follow-up period, each group had significantly lower quality of life scores and more severe dyspeptic symptoms and functional disability than controls, but did not differ

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significantly from each other; both groups were significantly more likely than controls to meet criteria for an anxiety disorder. At time of follow-up, use of acid suppression medication was significantly greater in the group with histologic evidence for esophagitis, compared with patients that had normal histology findings when the study began.

Conclusion—Among pediatric patients with dyspepsia evaluated by endoscopy and biopsy, those with histologic evidence for esophagitis or normal histology findings are at increased risk for chronic dyspeptic symptoms, anxiety disorder, and reduced quality of life in adolescence and young adulthood.

Keywords

gastroesophageal reflux; functional dyspepsia

Background

Gastroesophageal reflux disease (GERD) affects children as well as adults and carries the highest economic cost of any gastrointestinal illness in the United States [1]. In adults, GERD is appreciated as a chronic disease that may be progressive over time [2–3]. Several retrospective studies of adult patients with GERD have identified childhood GERD to be a risk factor for GERD in adulthood [4–6]. However, most pediatricians believe that the majority of infants with GERD “outgrow” their symptoms by one year of age, even though mucosal histology may remain abnormal [7–11]. The few pediatric studies that have followed pediatric GERD patients beyond infancy have yielded conflicting results regarding outcomes [12–16]. To date, no studies have followed children with GERD prospectively into adolescence and adulthood to assess their health outcomes.

Treatment of dyspeptic symptoms with acid suppressant medication may increase the risk for enteric infections, pneumonia, fractures, and micronutrient deficiencies [17–18]. Untreated GERD, however, is associated with serious complications such as esophageal ulcerations, peptic stricture, Barrett's esophagus, adenocarcinoma and extraesophageal disease [19]. Thus, it is important to know the extent to which dyspeptic symptoms and use of acid suppression persist beyond childhood, with the ultimate goal to develop treatment strategies that can minimize both complications of GERD and long term use of acid suppression [20].

Consensus statements emphasize the importance of symptom report and quality of life as indicators of outcome for GERD and functional dyspepsia (FD) [21–23]. Both GERD and FD have been linked to poor quality of life among adults in the general population [24–26] and one study has linked pediatric GERD to poor quality of life [27]. In addition to an association with general measures of quality of life, dyspeptic symptoms and GERD have been associated with anxiety and depression in adults [28–30]. No studies have examined the association of dyspepsia or GERD to anxiety and depression in children.

This study aimed to describe the natural history of a prospective cohort of pediatric patients with dyspeptic symptoms who underwent upper endoscopy with biopsy as part of their pediatric gastroenterology subspecialty evaluation. Based on endscopy results, patients were classified into two groups – those with and those without histologic esophagitis.. Although dyspepsia with histologic esophagitis is associated with a diagnosis of GERD and dyspepsia with normal esophageal histology is associated with a diagnosis of FD[31], we described the groups more descriptively as dyspepsia with and without histologic esophagitis. Patients with and without histologic esophagitis were compared to healthy controls that also were followed prospectively.

Outcomes evaluated at follow-up in adolescence and young adulthood included severity of dyspeptic symptoms, use of acid suppression medication, quality of life, anxiety, and depression. The null hypothesis was that the reflux esophagitis, normal esophageal histology and control groups would not differ significantly on these variables at long-term follow-up.

Materials and Methods

Sample

The study entailed a secondary analysis of an existing database of pediatric patients and community controls. The patient sample was drawn from several studies conducted by Walker and colleagues between 1993 and 2004 [e.g. 32–33]. Consecutive new patients referred to Vanderbilt Pediatric Gastroenterology Clinic for evaluation of abdominal pain were eligible for those studies if they were between the ages of 8 and 16 years, had abdominal pain of at least 3 months' duration, no chronic illness or disability, living with at least one parent, and English speaking. Study participants were interviewed and completed questionnaires in the waiting room prior to the child's medical evaluation. Participants consented to be contacted regarding participation in future studies.

The subgroup of patients in the original studies whose medical evaluation included upper endoscopy with biopsies of the esophagus performed within six months of the initial clinic visit were eligible for the present study if their biopsies were normal or were consistent with reflux esophagitis. Histologic reflux esophagitis was defined by basal cell hyperplasia, spongiosis, and presence of intraepithelial eosinophils [34]. Patients with evidence of infectious esophagitis, duodenitis, peptic ulcer disease, chronic active gastritis, or villous blunting were excluded. Patients with more than twenty eosinophils per high power field were excluded due to possible overlap with eosinophilic esophagitis. Patients also were excluded if the medical evaluation resulted in a diagnosis of Crohn's disease, celiac disease, or other significant organic disease. *Helicobacter pylori* infection was not a reason for excluding patients with reflux esophagitis.

For the purposes of this study, dyspeptic symptoms included patient report of the following items on a symptom questionnaire: chest pain, abdominal pain, lump in throat, nausea, difficulty swallowing, vomiting, bloating, and food making you sick. Patients with fewer than two dyspeptic symptoms at initial evaluation were excluded from the follow-up study.

The healthy control sample for the current study was obtained from control samples in Walker and colleagues' prior studies during the same time period [e.g. 32–33]. Participants for those samples were recruited from community schools and were eligible for the present follow up study if they had no chronic illness and no abdominal pain in the month preceding initial study participation.

Procedure

Following approval of the Vanderbilt Institutional Review Board, participants were contacted by telephone or mail by the research coordinator. The coordinator described the study and scheduled an appointment to administer the study protocol by telephone. Parents of adolescent participants were given information about the study and gave consent for the adolescent to be contacted for assent. The follow up interval ranged from 5 to 15 years after the baseline assessment for the original study and was conducted during the years 2008–2011 when participants ranged in age from 12 to 32 years.

At the beginning of the phone interview, the experimenter confirmed consent and assent.. The experimenter administered self-report questionnaires orally and provided participants with response options for ratings as appropriate. The health services questionnaire was

completed by parents for participants less than 18 years of age. All interviews were audio recorded to allow review for accuracy. After completing the telephone interview, participants were sent the STAI-T and CES-D questionnaires to complete on-line or to return in written format.

Measures

The measures examined at baseline and follow-up are listed in Figure 1 and further described below:

Abdominal pain severity—The severity of abdominal pain was assessed with the patient-report Abdominal Pain Index [35]. This measure comprises five items assessing the frequency, duration, and intensity of abdominal pain episodes experienced during the previous 2 weeks. A total severity score, ranging from 0 to 4, is a composite of these ratings.

Dyspeptic symptom severity—Severity of dyspeptic symptoms was evaluated with 8 items from the Children's Somatization Inventory (CSI) that assess dyspeptic symptoms including chest pain, abdominal pain, nausea, vomiting, difficulty swallowing, lump in the throat, bloating, and food making you sick [36]. The stem for symptom report on the CSI is, "In the past two weeks, how much were you bothered by (*symptom*)?" The response format for each question is a 5-point scale ranging from "not at all" (0) to "a whole lot" (4). Responses to the eight dyspeptic scores were summed to calculate a total score for severity of dyspeptic symptoms.

Health services utilization questionnaire—A questionnaire regarding recent health service utilization was administered at follow-up as a self-report questionnaire for adult participants and as a parent-report questionnaire for participants under the age of 18 years. Participants were asked to report the use of prescription or over- the- counter acid suppression medication during the previous 3 months as well as any history of Nissen fundoplication. Participants also were asked if they had ever been diagnosed with inflammatory bowel or other GI disease by a physician or medical professional.

Psychological functioning—Depressive symptoms were assessed at baseline in the original studies with the Children's Depression Inventory (CDI), a validated self-report measure for children between 7– 17 years of age [37–38]. A total CDI score is computed with a higher score indicating greater severity of depressive symptoms. At follow-up, depressive symptoms were assessed with a validated self-report measure for adolescents and adults, the Center for Epidemiological Studies-Depression Scale (CES-D) [39]. The CES-D assesses the frequency of 20 depressive symptoms during the past week. Scoring is a simple sum of item responses with a higher score indicating greater severity of depressive symptoms. Also at follow up, the State-Trait Anxiety Inventory, Trait Form (STAI-T) was administered [40]. This validated 20-item self-report measure assesses the tendency to experience anxiety symptoms. Responses are summed to obtain a total score with a higher score indicating greater frequency and number of symptoms of anxiety.

In addition to self-report measures of anxiety and depression, a semi-structured psychiatric diagnostic interview -- the Anxiety Disorders Interview Schedule IV (ADIS) – was administered at follow up by trained mental health professionals to assess DSM-IV criteria for anxiety and mood disorders [41–42]. Anxiety disorders included separation anxiety, panic, agoraphobia, social anxiety, generalized anxiety disorder, obsessive compulsive disorder, specific phobia, post-traumatic stress disorder, or anxiety disorder not otherwise specified. Mood disorders included major depressive disorder, dysthmia, or depressive disorder not otherwise specified. Participants were evaluated for current presence of each disorder as

well as lifetime history of the disorder. For participants under 18 years, the participant and a parent were interviewed separately and results were collated to determine whether the participant met diagnostic criteria for any psychiatric disorder. The interviewer was blind to the health status of participants.

Quality of life—Health-related impairment in activities, an aspect of quality of life, was assessed both at baseline and at follow-up with the Functional Disability Inventory (FDI) [43–44]. This validated self-report measure assesses difficulty in physical and psychosocial functioning due to physical health during the previous two weeks. Respondents rate 15 items on a 5-point scale, ranging from (0) *no trouble* to (4) *impossible*, and these ratings are summed to yield a total score that can range from 0 to 60. Higher scores indicate greater disability.

At follow-up, an additional measure of health-related quality of life also was administered. The Short Form Health Survey (SF-36) is a 36-item self-report questionnaire that assesses eight dimensions of health: 1) limitations in physical activities because of health problems; 2) limitations in social activities due to physical or emotional problems; 3) limitations in usual role activities because of physical health problems; 4) bodily pain; 5) general mental health including psychological distress and well-being; 6) limitations in usual role activities because of emotional problems; 7) vitality including energy and fatigue; and 8) general health perceptions [45]. The eight scales are aggregated to create two component scores, the physical component score (PCS) and mental component score (MCS). A total summary score is also calculated.

Demographic variables—Demographic information collected at baseline and follow-up included gender, date of birth, racial and ethnic group identification, and living circumstances.

Medical Records including clinic notes, gross endoscopic findings, pathology report, laboratory data and imaging were retrospectively reviewed.

Statistical Methods

Fischer's exact test and chi-square analyses were used to detect significant group differences on the nominal outcome variables. Analysis of variance between groups (ANOVA) and t-tests were used to compare the continuous outcome measures between groups. The Scheffe method was used for multiple comparisons between the three groups within the ANOVA. Subgroup analyses adjusted for gender. Logistic regression was used to evaluate whether baseline characteristics predicted the use of acid suppression at follow-up. A p-value less than 0.05 was considered significant. Data were analyzed using SPSS for Windows Version 19 statistical package (SPSS, Inc., Chicago, IL).

Results

Figure 2 describes patient recruitment and the study timeline. Seven patients who underwent upper endoscopy but endorsed fewer than two dyspeptic symptoms were excluded. Based on review of medical records, four patients with Crohn's disease and one with cholelithiasis also were excluded. Thus, the final sample consisted of 183 pediatric patients with two or more dyspeptic symptoms who underwent endoscopy with biopsies. Of those whose upper endoscopy exhibited histologic reflux esophagitis, 50 participated in follow-up. Of those with normal biopsies at baseline, 53 participated in follow-up. In the control group, one participant was excluded from due to pregnancy at the time of follow-up, leaving a final sample of 142 participants in the control group.

Baseline variables including age, gender, race, dyspeptic symptoms, depression, and disability are presented in Table 1. At baseline, both the esophagitis and normal histology groups had more severe dyspeptic symptoms, abdominal pain, and functional disability compared to the controls but did not differ from each other on any variable. There was a statistically significant difference in age between the normal histology and controls at baseline but no significant age difference between any other groups.

The average follow-up interval was 7.6 years. The follow up interval for the control group (6.9 years) was significantly shorter than that for the reflux esophagitis and normal histology groups (8.3 and 9.0 years, respectively) which did not differ significantly from each other. The mean age of the control group at follow-up, (18.3 years) was significantly younger than the reflux esophagitis group (20.3 years) and the normal histology group (21.6 years) which did not differ significantly from each other.

As shown in Table 2, the groups differed significantly in use of acid suppression medication at follow-up. The reflux esophagitis group was more likely to use acid suppressants than the normal histology group which, in turn, was significantly more likely to use acid suppressants than the control group. Two participants in the reflux esophagitis group reported a history of Nissen fundoplication but no participants in the other groups reported having had this procedure. The reflux esophagitis and normal histology groups had similar severity of dyspeptic symptoms and both groups had significantly higher symptom severity compared to controls.

Table 3 presents measures of quality of life and psychological functioning at follow up. Both the reflux esophagitis and normal histology groups reported poorer overall health related quality of life and higher levels of functional disability at follow up compared to controls. However, the esophagitis and normal endoscopy groups did not differ significantly from each other on quality of life measures at follow up. The normal histology group, but not the esophagitis group, endorsed significantly higher levels of depression and anxiety as well as significantly reduced quality of life on the SF-36 mental health dimension at follow up compared to the control group.

Psychiatric diagnostic interviews (Table 4) indicated that significantly more patients in the esophagitis group (28%) met criteria for a current anxiety disorder at follow up compared to controls (13.6%). Both the esophagitis and normal histology groups were significantly more likely to have met diagnostic criteria for anxiety disorders and mood disorders during their lifetimes compared to controls.

Finally, we compared characteristics of the individuals on acid suppression therapy at follow-up (n=80) to see if they differed from those not on acid suppression at follow up (n=22), regardless of previous histologic findings. Controls were excluded from this analysis. Individuals on antacids at follow up had significantly more dyspeptic symptoms compared to those not on antacids at follow up (CSI dyspeptic score, mean 6.0 vs. 3.9, $p< 0.05$) but did not differ on severity of abdominal pain at follow up (API mean, 1.16 vs. 1.45, $p>0.05$). SF-36 scores indicated that quality of life was poorer in those on antacids at follow up compared to those not on antacids (SF-36 total 69.2 vs. 79.8, $p<0.05$). Those using antacids at follow up reported higher anxiety and depression than those not using antacids, but this difference did not reach statistical significance (CESD sum depression 13.4 vs. 9.4, $p=0.054$; STAI-T 16.8 vs. 21.71, $p=0.053$). We performed binary logistic regression analysis to assess predictors for acid suppression use at follow-up. The model included baseline gender, age, histology findings, abdominal pain, dyspeptic symptoms, functional disability, and depression score. None of these variables were significant predictors of the use of acid suppression at follow-up.

Conclusion

This prospective cohort study of pediatric patients evaluated with upper endoscopy makes two important contributions to the literature. First, we found that these pediatric patients with dyspeptic symptoms, both with and without abnormal esophageal histology, had more dyspeptic symptoms, greater functional disability, and poorer health related quality of life compared to controls in adolescence and young adulthood. Related studies have reported poorer health related quality of life in clinical and community samples of adults with GERD and with dyspepsia [46, 24–26]. Ours is the first study to show that pediatric patients with dyspeptic symptoms evaluated by endoscopy are at increased risk of reduced quality of life later in their development and that this risk applies equally to patients with and without histologic esophagitis. This finding suggests that, for many pediatric patients evaluated with endoscopy in the tertiary care setting, dyspepsia may become a chronic condition that negatively impacts their daily lives as they transition to adulthood.

Our second important finding is a strong association between pediatric dyspepsia and anxiety. Results of a psychiatric diagnostic interview by a trained clinician blind to participants' health status indicated that, at the time of follow up in adolescent and young adulthood, approximately half of both the esophagitis and normal histology patients had a lifetime history of one or more anxiety disorders and a quarter currently met criteria for an anxiety disorder at follow up. These rates of lifetime and current anxiety disorders were double those observed in the control group. The esophagitis and normal histology groups also had elevated rates of lifetime depressive disorders but both they and controls had very low current levels of depressive disorders at follow up. Whereas other studies have linked self-reported symptoms of anxiety and depression to GER and FD, ours is the first to demonstrate, using a psychiatric diagnostic interview, that these symptoms reached clinical significance [28–30,47]. Our findings also suggest that depressive symptoms may resolve or be episodic in youth with dyspepsia, while anxiety appears to be more chronic.

Anxiety and depression could develop as a consequence of living with chronic dyspeptic symptoms that are poorly controlled by treatment. Clinical studies suggest that, in GERD patients, anxiety rather than disease pathology may lead to poorer quality of life and worsened symptom severity [48–50]. It also is possible that anxiety and depression affect clinical outcomes directly by impacting adherence to provider recommendations regarding diet, lifestyle, and medication. Anxiety and depression also may reflect central sensitization of pain and dysregulation of reciprocal communication between the brain and the gut, a factor that is increasingly recognized to play an important role in the pathophysiology of functional GI disorders [51–53]. For example, a recent study by Sharma found that anxiety induction increased hyperalgesia to acid infusion in healthy volunteers, likely through central sensitization [54].

The only significant difference at follow-up between those with and without baseline histological esophagitis was greater reported use of acid suppression medication by those with esophagitis. These results regarding use of acid suppression medication are consistent with those of Hyam's study which reported similar percentages of children on acid suppression at a shorter follow up (24% with normal endoscopy and 26% with abnormal endoscopy). This observation suggests that histology alone is not adequate to discriminate between organic and functional dyspepsia.

In this study, we classified patients with dyspeptic symptoms into two groups – those with histologic evidence of reflux esophagitis and those with normal histology -- based on findings of upper endoscopy and biopsy. Hyams and colleagues used a similar procedure for classifying patients in their study [16]. As they noted, upper GI inflammation often occurs in

asymptomatic adults and, without comparable data for asymptomatic children, we cannot rule out the possibility that mucosal inflammation was unrelated to dyspeptic symptoms in our pediatric sample. It also is possible that alternative criteria for classifying patients, for example, based on results of a pH probe or symptom response to a trial of acid suppression, would have classified our patients differently [55].

Important limitations of the study include the highly selected patient sample, absence of information regarding treatment during the follow up interval, loss of some patients to follow-up, and lack of medical evaluation with upper endoscopy and esophageal biopsy at follow up. Patients evaluated with endoscopy at a tertiary care center may differ substantially from nonreferred youth with dyspepsia; study findings cannot be generalized to those youth. Moreover, without repeat endoscopy, it is not possible to know whether patients' lack of improvement over time may have been due to worsening of disease or a change in underlying diagnosis. Additional limitations are related to advances in clinical practice that have occurred since these patients were evaluated (1993–2004). For example, recent consensus guidelines have put emphasis on mucosal breaks as a finding suggestive of reflux esophagitis [56]. This was not a finding commonly described at the time when the endoscopies were done in our study patients; whether study patients with or without esophagitis had mucosal breaks is unknown to us. The use of multichannel impedence monitoring is another advance not available at the time of evaluation; this technique might have yielded evidence of nonacid reflux in some patients.

This study is the largest prospective cohort of its kind to describe the natural history of pediatric dyspepsia with and without positive histologic findings. The five to fifteen year length of follow-up is considerably longer than that for any previous study and allowed us to examine outcomes for children with dyspepsia in adolescence and young adulthood. Of particular note, the study included a control group that also was followed prospectively. Finally, the use of validated measures strengthens confidence in our findings.

An interesting clinical implication of this study is that, within the pediatric subspecialty setting, pediatric patients with and without positive histology associated with dyspeptic symptoms may be at equally increased risk for long term persistence of their symptoms and reduced quality of life. These findings further blur the distinction between organic and functional gastrointestinal disorders [57]. Our evidence linking anxiety disorder to dyspepsia with and without positive histology suggests that pediatric gastroenterologists should consider evaluation of psychological functioning as an integral part of the medical evaluation for dyspeptic symptoms. Research is needed to identify factors in childhood that may be prognostic indicators of long term outcomes of pediatric dyspepsia. Finally, treatment studies are needed to evaluate the extent to which reduction in anxiety may be associated with reductions in dyspeptic symptoms and vice versa.

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Abbreviations

FD	functional dyspepsia
GERD	gastroesophageal reflux disease

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Baseline Measures	Follow-Up Measures
Abdominal Pain Index	Abdominal Pain Index
Children's Somatization Inventory	Child/Adult Somatization Inventory
Children's Depression Inventory	Rome III Modular Questionnaire
Functional Disability Index	Health Questionnaire
Medical Records	Functional Disability Index
Demographics	Short Form Health Survey
	Center for Epidemiological Studies-Depression Scale
	State-Trait Anxiety Inventory, Trait Form
	Anxiety Disorders Interview Schedule IV
	Medical Records
	Demographics

Figure 1.
Measures Administered at Baseline and Follow-Up

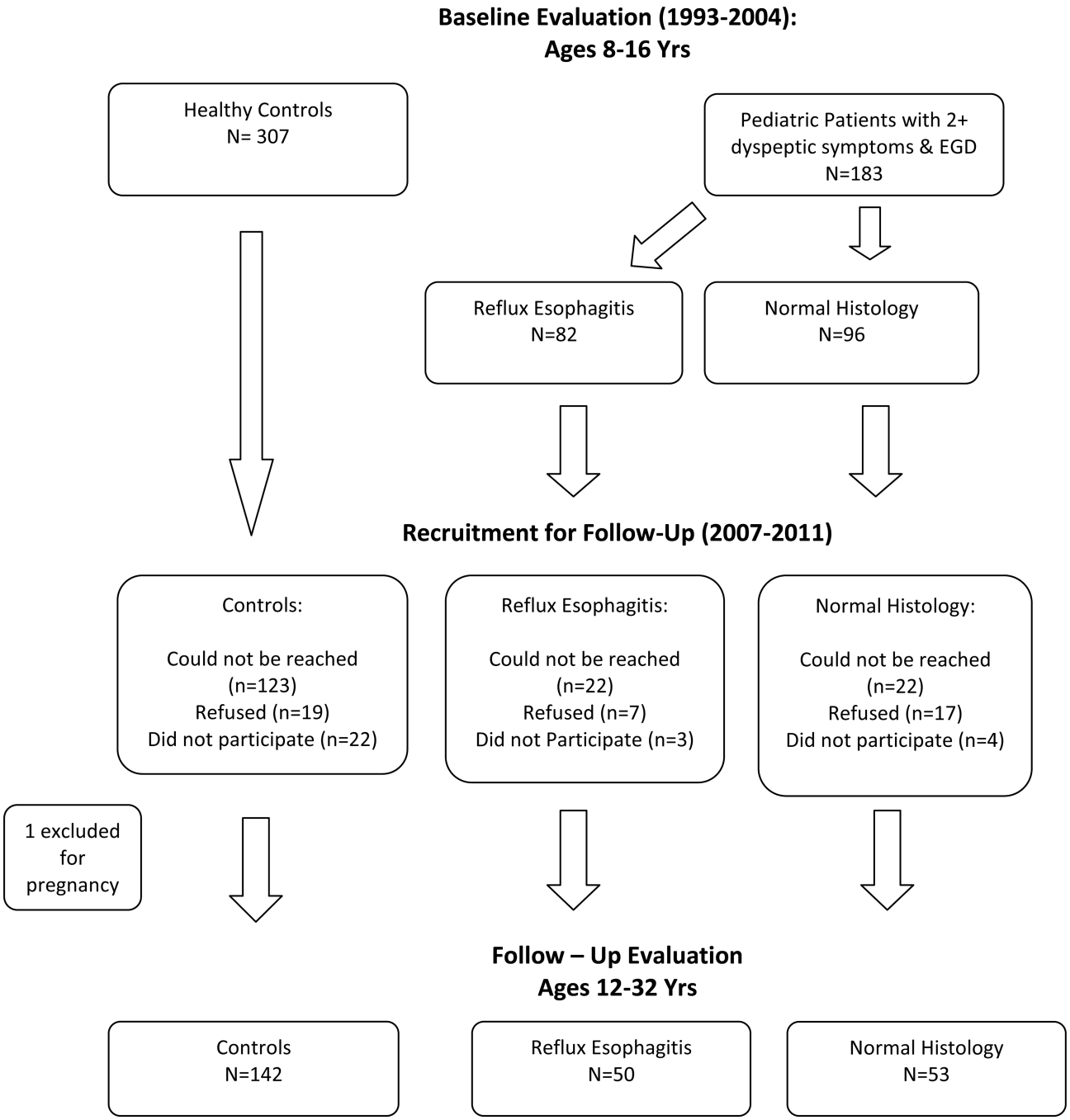

Figure 2.
Study Timeline & Participant Recruitment

Table 1

Measures at Baseline by Reflux Esophagitis, Normal Histology, and Control Group

	Reflux Esophagitis (n=50)	Normal Histology (n=53)	Controls (n=142)	p-value GER vs. FD	p-value GER vs. Control	p-value FD vs. Control
Mean Age in Years mean ± SD	11.58 ± 2.43	11.98 ± 2.55	10.96 ± 2.11	NS	NS	<0.05
Gender (% female)	48 % (24/50)	68% (36/53)	56% (79/142)	NA	NA	NA
Race (% white)	94% (47/50)	89% (47/53)	96% (135/141)	NA	NA	NA
Intact Family (% live both parents)	60% (30/50)	62% (33/53)	46% (65/142)	NA	NA	NA
Dyspeptic Severity (CSI) mean ± SD	9.96 ± 4.79	9.42 ± 4.58	2.67 ± 3.72	NS	<0.001	<0.001
Abdominal Pain Severity (API); mean ± SD	2.16 ± 0.81	2.08 ± 0.83	0.65 ± 0.79	NS	<0.001	<0.001
Depressive Score (CDI) mean ± SD	8.76 ± 5.89	8.77 ± 7.71	NA	NS	NA	NA
Functional Disability (FDI)[a]; mean ± SD	11.05 ± 8.80	9.15 ± 8.22	4.26 ± 5.58	NS	<0.001	<0.001

[a] Child Report FDI not available for all subjects (Reflux Esophagitis=39, Normal Histology=33, Control=82)

Note: CSI= Children's Somatization Inventory; API= Abdominal Pain Index; CDI= Children's Depression Inventory; FDI= Functional Disability Inventory; NS= not significant; NA= not applicable

Table 2

Symptom Related Measures at Follow-Up by Reflux Esophagitis, Normal Histology, and Control Group

	Reflux Esophagitis (n=50)	Normal Histology (n=53)	Controls (n=142)	p-value Reflux vs. Normal	p-value Reflux vs. Control	p-value Normal vs. Control
Self Reported Outcomes						
Acid Suppression Use	31% (15/49)	13% (7/53)	4% (5/142)	<0.05	<0.05	<0.001
Nissen Fundoplication	4% (2/50)	0% (0/53)	0% (0/142)	NA	NA	NA
Dyspeptic Symptom Severity mean ± SD	4.80 ± 3.99	3.96 ± 3.65	1.96 ± 2.25	NS	<0.001	<0.001
Abdominal Pain Severity mean ± SD	1.16 ± 1.00	1.28 ± 1.02	0.45 ± 0.60	NS	<0.001	<0.001

Note: NS= not significant; NA= not applicable; GI= Gastrointestinal

Table 3

Quality of Life and Psychological Functioning at Follow-Up by Reflux Esophagitis, Normal Histology, and Control Group

Measure	Reflux Esophagitis (n=50)	Normal Histology (n=53)	Controls (n=142)	p-value Reflux vs. Normal	p-value Reflux vs. Control	p-value Normal vs. Control
HRQOL, Total Total SF-36; mean ± SD	78.82 ± 15.69	75.79 ± 14.33	84.97 ± 9.37	NS	<0.05	<0.001
HRQOL, Physical Component SF-36 PCS; mean ± SD	76.28 ± 17.50	72.25 ± 15.60	83.71 ± 9.17	NS	<0.05	<0.001
HRQOL, Mental Component SF-36 MCS; mean ± SD	75.89 ± 15.38	72.91 ± 15.60	81.22 ± 12.17	NS	NS	<0.05
Functional Disability (FDI), mean ± SD	4.49 ± 6.21	5.02 ± 6.25	1.73 ± 3.08	NS	<0.05	<0.001
Depression (CES-D) mean ± SD	9.00 ± 7.70	11.17 ± 9.93	7.6 ± 6.78	NS	NS	<0.05
Anxiety (STAI-T) mean ± SD	16.98 ± 9.26	18.89 ± 10.89	13.19 ± 9.12	NS	NS	<0.05

Note: HRQOL= Health Related Quality of Life; SF-36= Short Form Health Survey; PCS: Physical Component Score; MCS: Mental Component Score; FDI= Functional Disability Inventory; CES-D= Center for Epidemiological Studies-Depression Scale; STAI-T= State-Trait Anxiety Inventory, Trait Form; NS= not significant; NA= not applicable

Table 4

Psychiatric Disorders at Follow-Up by Reflux Esophagitis, Normal Histology, and Control Group

	Reflux Esophagitis (n=50)	Normal Histology (n=53)	Controls (n=142)	p-value Reflux vs. Normal	p-value Reflux vs. Control	p-value Normal vs. Control
Current						
Anxiety Disorder	28.3% (13/46)	24.5% (13/53)	13.6% (19/140)	NS	<0.05	NS
Mood Disorder	6.5% (3/46)	7.5% (4/53)	2.9% (4/140)	NA	NA	NA
Lifetime						
Anxiety Disorder	43.5% (20/46)	54.7% (29/53)	23.6% (33/140)	NS	<0.05	<0.001
Mood Disorder	34.8% (16/46)	49.1% (26/53)	20.0% (28/140)	NS	<0.05	<0.001

Note: Current and Lifetime Anxiety and Mood Disorder criteria based upon The Anxiety Disorders Interview (ADIS), Schedule-IV; GER= gastroesophageal reflux; FD= functional dyspepsia