Table 1: Demographic and clinical characteristics of participants.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Marfan (N=801)** | **Other/autoimmune (n=146)** | **Classical EDS (n=313)** | **Hypermobility EDS (n=1574)** | **Vascular EDS (n=72)** | **Other/ Unknown EDS (n=212)** |
| **Age (years, SD)** | 43 (14) | 44 (15) | 43 (14) | 40 (13) | 42 (12) | 42 (14) |
| **Female (%)** | 61 | 80 | 91 | 95 | 83 | 93 |
| **Race (%)** |  |  |  |  |  |  |
| White | 87 | 95 | 93 | 92 | 89 | 87 |
| Black or African-American | 2 | 1 | 0 | 0 | 1 | 1 |
| Asian | 3 | 1 | 0 | 1 | 0 | 1 |
| Hispanic or Latino | 4 | 1 | 2 | 2 | 3 | 1 |
| Other | 4 | 1 | 2 | 6 | 7 | 9 |
| **Relationship (%)** |  |  |  |  |  |  |
| Single, never married | 29 | 24 | 25 | 28 | 22 | 27 |
| Married or domestic partnership | 61 | 60 | 60 | 60 | 53 | 58 |
| Divorced, separated, or widowed | 10 | 16 | 15 | 13 | 25 | 15 |
| **Education (%)** |  |  |  |  |  |  |
| Some high school or high school graduate | 13 | 10 | 11 | 10 | 15 | 14 |
| Some college or college graduate | 60 | 60 | 60 | 61 | 57 | 64 |
| Graduate degree | 27 | 30 | 29 | 30 | 28 | 23 |
| **How diagnosed (%)** |  |  |  |  |  |  |
| Genetic test (private sector) | 3 | 1 | 2 | 2 | 4 | 2 |
| Genetic test (MD) | 24 | 5 | 16 | 8 | 60 | 10 |
| Diagnosed clinically | 64 | 71 | 76 | 85 | 32 | 72 |
| N/A | 9 | 23 | 6 | 6 | 4 | 16 |
| **Sigmoidoscopy or colonoscopy if aged ≥50** | 74 | 83 | 81 | 80 | 68 | 85 |

Table 2: Cumulative incidence rates of specific gastrointestinal and cardiovascular manifestations among respondents with HCTDs.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Marfan (N=801)** | **Classical EDS (n=313)** | **Hypermobility EDS (n=1574)** | **Vascular EDS (n=72)** | **Other/ Unknown EDS (n=212)** | **Other/ autoimmune (n=146)** | **p heterogeneity** |
| **Perforation following endoscopy (%, 95% CI)** | 0 (0% to 1.3%) | 0.6% (0% to 1.8%) | 0.6% (0.2% to 1.4%) | 9.4% (2.0% to 25.0%) | 1.8% (0.2% to 6.5%) | 1.6% (0% to 8.4%) | p < 0.001 |
| **Spontaneous intestinal perforation (%, 95% CI)** | 2.2% (1.2% to 3.5%) | 5.4% (3.0% to 8.7%) | 4.5% (3.4% to 5.7%) | 26.9% (16.8% to 39.1%) | 9.1% (5.2% to 14.6%) | 5.2% (1.9% to 10.9%) | p < 0.001 |
| **Diverticulosis (%, 95% CI)** | 10.9% (8.7% to 13.4%) | 24.3% (19.3% to 29.8%) | 17.0% (15.1% to 19.1%) | 33.3% (21.4% to 47.1%) | 22.7% (16.5% to 29.9%) | 19.8% (12.7 to 28.7%) | p < 0.001 |
| **Colonic polyps (%, 95% CI)** | 27.7% (22.4% to 33.4%) | 21.7% (15.6% to 28.9%) | 22.8% (19.8% to 26.1%) | 15.6% (5.3% to 32.8%) | 30.2% (21.7% to 39.9%) | 20.0% (11.1 to 31.8) | p = 0.22 |
| **Cardiovascular manifestations (%, 95% CI)** | 78.1% (74.8% to 81.1%) | 36.8% (31.0% to 42.8%) | 25.9% (23.5% to 28.4%) | 40.3% (28.5% to 53.0%) | 42.0% (34.2% to 50.2%) | 37.8% (28.8% to 47.5%) | p < 0.001 |

Supplemental Table 1: National and regional patient groups that provided electronic mailing lists.

|  |  |
| --- | --- |
| **Included** | **Contacted but did not respond** |
| Massachusetts Chapter of the National Marfan Foundation | Center for Ehlers Danlos Syndrome Alliance (CEDSA) |
| National Marfan Foundation | EDS Cares Network |
| EDS New England/Massachusetts Support Group |  |
| Ehlers-Danlos National Foundation (EDNF) |  |
| EDS Awareness.com |  |
| EDSr's United |  |

Supplemental Figure 1: Flowchart of participant responses.

2171 EDS

146 Other CTD

3934 Respondents

801 MFS

626 Age <18 years or missing

141 Spouses

49 Disease missing or rare:

17 missing

31 Loeys-Dietz syndrome

1 osteogenesis imperfecta

313 Classical

1574 HT

72 Vascular

212 Unknown

3118 Eligible Respondents

Supplemental Table 2: Questionnaire items

**The next questions are about colorectal cancer screening.**

I am 50 or older.

I am 49 or younger.

A blood stool test is a test that may use a special kit at home to determine whether the stool contains blood. Have you ever had this test using a home kit?

Sigmoidoscopy and colonoscopy are exams in which a tube is inserted in the rectum to view the colon for signs of cancer or other health problems. Have you ever had either of these exams?

For a sigmoidoscopy, a flexible tube is inserted into the rectum to look for problems.

A colonoscopy is similar, but uses a longer tube, and you are usually given medication through a needle in your arm to make you sleepy and told to have someone else drive you home after the test. Was your MOST RECENT exam a sigmoidoscopy or a colonoscopy?

Sometimes patients undergo a procedure called a virtual colonoscopy for colon cancer screening. This is when a small tube is inserted into the rectum to inflate the intestine and then you undergo a CT scan. Have you had colon cancer screening with a virtual colonoscopy?

Sometimes patients undergo a procedure called a barium enema for colon cancer screening. This involves the injection of a liquid and/or air into your rectum through a small tube and then undergoing an x-ray. Have you had colon cancer screening with a barium enema?

One rare complication of a colonoscopy, virtual colonoscopy, flexible sigmoidoscopy, or other colon cancer screening is ‘bowel perforation,’ when the tube accidentally makes a hole or tear in your gut wall. Did you have this complication from your procedure?

**Separate Gastrointestinal Section**

Have you ever had pre cancerous polyps?

Have you ever had diverticulosis (small outpouchings in your colon)?

Have you ever had diverticulitis (infection of the small outpouchings in your colon)?

Have you ever had a perforation of your intestine (hole in the wall of any parts of your intestine, including the esophagus or colon)