Epidemiology of IBD in Pediatric Patients in the US: Data from the ImproveCareNow Registry

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Overview

- ImproveCareNow
- Age, disease type and severity, use of medications
- Sequential use of biologics
- Example study population diagrams
ImproveCareNow Learning Health Network

- Founded in 2007
  - 109 sites (97 in US)
  - 950 pediatric gastroenterologists
  - >85% of patients enrolled
- Sites pay annual participation fee and provide site staffing
- Registry
  - 35,000 patients
  - 250,000 visits
  - 80,000 patient-years

- Collect 50 – 75 data elements at each OP visit
  - Symptoms
  - Physical findings
  - Medications
  - Assessment of disease phenotype, extent, severity
  - PGA, Short PCDAI, PUCAI, Mayo subscore (SF, RB)
- Brief CRF for hospitalized patients
- Data used for clinical care, improvement and research
Analysis

- Given size of ICN population and diversity of centers, patients are broadly representative of US pediatric IBD population (opinion)
- Young adults followed at pediatric centers may not be representative of young adult IBD population
  - Analyses limited to patients/visits prior to 18 years of age
- ICN not an inception cohort
  - No data collected about disease severity, phenotype, medication use prior to ICN enrollment
## Age at diagnosis

<table>
<thead>
<tr>
<th>Age group</th>
<th>CD n=21,150 (63%)</th>
<th>UC n=9,549 (29%)</th>
<th>IBD NOS n=2,793 (8%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2</td>
<td>205 (1%)</td>
<td>111 (1%)</td>
<td>75 (3%)</td>
</tr>
<tr>
<td>2 to &lt;6</td>
<td>1,149 (5%)</td>
<td>1,004 (11%)</td>
<td>345 (12%)</td>
</tr>
<tr>
<td>6 to &lt;12</td>
<td>7,959 (38%)</td>
<td>3,043 (32%)</td>
<td>928 (33%)</td>
</tr>
<tr>
<td>12 to &lt;18</td>
<td>11,837 (56%)</td>
<td>5,391 (57%)</td>
<td>1,445 (52%)</td>
</tr>
</tbody>
</table>
## Age at most recent visit

<table>
<thead>
<tr>
<th>Age group</th>
<th>CD n=8,960 (67%)</th>
<th>UC n=3,640 (27%)</th>
<th>IBD NOS n=853 (6%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2</td>
<td>13 (0.1%)</td>
<td>7 (0.2%)</td>
<td>3 (0.4%)</td>
</tr>
<tr>
<td>2 to &lt;6</td>
<td>140 (2%)</td>
<td>89 (2%)</td>
<td>62 (7%)</td>
</tr>
<tr>
<td>6 to &lt;12</td>
<td>1,638 (18%)</td>
<td>754 (21%)</td>
<td>245 (29%)</td>
</tr>
<tr>
<td>12 to &lt;18</td>
<td>7,169 (80.0%)</td>
<td>2,790 (77%)</td>
<td>543 (64%)</td>
</tr>
</tbody>
</table>

Analysis includes patients with a recorded visit in 2017
Age at diagnosis vs current age (all IBD)
Age at diagnosis over time (CD)
Age at diagnosis over time (UC)
Disease Type at last recorded visit

Analysis includes 13,453 patients <18 years with a recorded visit in 2017
Disease Type at last recorded visit

- < 2
  - CD: 30%
  - UC: 13%
  - IBD NOS: 57%
  - n=23

- 2 to <6
  - CD: 48%
  - UC: 31%
  - IBD NOS: 21%
  - n=291

- 6 to <12
  - CD: 29%
  - UC: 9%
  - IBD NOS: 62%
  - n=2,637

- 12 to <18
  - CD: 27%
  - UC: 5%
  - IBD NOS: 68%
  - n=10,502
CD disease severity by sPCDAI

DISEASE ACTIVITY

- Inactive: 42%
- Mild: 23%
- Moderate: 14%
- Severe: 21%

Worst ever recorded in Registry (n=8,520)

DISEASE ACTIVITY

- Inactive: 79%
- Mild: 12%
- Moderate: 5%
- Severe: 4%

Last recorded visit in 2017 (n=6,460)
CD disease severity by sPCDAI
Most recent recorded in 2017

- Inactive
- Mild
- Moderate
- Severe

- < 2
  - n=7
  - 86%
  - 14%

- 2 - <6
  - n=99
  - 82%
  - 12%
  - 3%

- 6 - <12
  - n=1,212
  - 80%
  - 13%
  - 4%
  - 3%

- 12 - <18
  - n=5,142
  - 79%
  - 12%
  - 5%
  - 4%
UC disease severity by PUCAI

Worst ever recorded in Registry (n=3,567)

Last recorded visit in 2017 (n=3,399)
UC disease severity by PUCAI
Most recent recorded in 2017
### Prednisone use

<table>
<thead>
<tr>
<th></th>
<th>Ever recorded n (%)</th>
<th>Recorded at last visit in 2017 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD n=8,960</td>
<td>2,999 (34%)</td>
<td>396 (4%)</td>
</tr>
<tr>
<td>UC n=3,640</td>
<td>1,615 (44%)</td>
<td>325 (9%)</td>
</tr>
<tr>
<td>IBD NOS n=853</td>
<td>349 (41%)</td>
<td>72 (8%)</td>
</tr>
</tbody>
</table>

Analysis include patients with one or more visits in 2017 who were <18 years of age at their last visit.
# 6MP, Azathioprine, or MTX use

<table>
<thead>
<tr>
<th></th>
<th>Ever recorded n (%)</th>
<th>Recorded at last visit in 2017 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CD n=8,960</strong></td>
<td>5256 (59%)</td>
<td>3506 (39%)</td>
</tr>
<tr>
<td><strong>UC n=3,640</strong></td>
<td>1562 (43%)</td>
<td>1056 (29%)</td>
</tr>
<tr>
<td><strong>IBD NOS n=853</strong></td>
<td>365 (43%)</td>
<td>240 (28%)</td>
</tr>
</tbody>
</table>

Analysis include patients with one or more visits in 2017 who were <18 years of age at their last visit.
### Biologic use (anti-TNF, ustekinumab, vedolizumab)

<table>
<thead>
<tr>
<th></th>
<th>Ever recorded n (%)</th>
<th>Recorded at last visit in 2017 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CD</strong> n=8,960</td>
<td>5991 (67%)</td>
<td>5152 (56%)</td>
</tr>
<tr>
<td><strong>UC</strong> n=3,640</td>
<td>1372 (38%)</td>
<td>1170 (32%)</td>
</tr>
<tr>
<td><strong>IBD NOS</strong> n=854</td>
<td>317 (37%)</td>
<td>246 (29%)</td>
</tr>
</tbody>
</table>

Analysis includes patients with one or more visits in 2017 who were <18 years of age at their last visit.
Use of sequential biologic agents

- Study using data from the ImproveCareNow registry
  - January 2008 to September 2016
  - 17,639 patients diagnosed with IBD before age 18
  - Sponsored by Takeda

- A subset of 1,029 patients who received their first biologic dose after enrollment into ICN had a chart review at 39 ICN centers in the US to obtain additional clinical information
  - Use and timing of medications prior to enrollment in ICN
Use of sequential biologic agents

- Median time from diagnosis to 1st biologic agent:
  - CD: 325 days
  - UC: 425 days
- The first biologic agent was an anti-TNF agent in 100% of cases

Kaplan J, et al. Gastroenterology 2018;154: S669
# Persistence on 1\textsuperscript{st} anti-TNF

<table>
<thead>
<tr>
<th>Group</th>
<th>CD</th>
<th>UC</th>
</tr>
</thead>
<tbody>
<tr>
<td>% remaining on 1\textsuperscript{st} anti-TNF:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 months</td>
<td>85%</td>
<td>75%</td>
</tr>
<tr>
<td>24 months</td>
<td>79%</td>
<td>66%</td>
</tr>
<tr>
<td>36 months</td>
<td>74%</td>
<td>55%</td>
</tr>
</tbody>
</table>

Most common reasons for discontinuation:

- Loss of response: 40%, 37%
- Intolerance: 26%, 16%
- 1\textsuperscript{st} non-response: 15%, 29%

Frequency of multiple biologic agent use in biologic agent exposed patients

<table>
<thead>
<tr>
<th># BAs used&lt;sup&gt;c&lt;/sup&gt;</th>
<th>% of IBD patients</th>
<th>% of CD patients</th>
<th>% of UC patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 2</td>
<td>17%</td>
<td>16%</td>
<td>20%</td>
</tr>
<tr>
<td>≥ 3</td>
<td>2%</td>
<td>2%</td>
<td>3%</td>
</tr>
</tbody>
</table>

<sup>c</sup> Median follow up = 1.56 years (IQR: 0.89 – 2.57 years)
Example CD trial population diagram

All patients in registry  
\( n = 35,616 \)

- Activated  
  \( n = 20,781 \)
  - Age 0 - <18  
    \( n = 13,797 \)
    - Crohn's disease  
      \( n = 8,616 \)
      - Moderate or severe disease  
        \( n = 2,710 \)
    - Not Crohn's disease  
      \( n = 5,181 \)
      - Moderate or severe disease  
        \( n = 5,906 \)
  - Deactivated  
    \( n = 14,385 \)
    - Age \( \geq 18 \)  
      \( n = 6,984 \)

Visit in 2017  
\( n = 2,579 \)

- Moderate or severe disease in 2017  
  \( n = 1,040 \)
- No moderate or severe disease in 2017  
  \( n = 1,539 \)

No visit in 2017  
\( n = 131 \)

Prior treatment with prednisone, IM +/or ATNF  
\( n = 792 \)

- No prior treatment with prednisone, IM +/or ATNF  
  \( n = 248 \)

No ileostomy in last 12 months or abdominal surgery ever  
\( n = 749 \)

Ileostomy in last 12 months or abdominal surgery ever  
\( n = 43 \)
CD trial population stratified by age and ATNF use

Crohn's disease \( n = 749 \)

<table>
<thead>
<tr>
<th>Age (Yr)</th>
<th>No (n, %)</th>
<th>Yes (n, %)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0</td>
</tr>
<tr>
<td>2 - &lt;6</td>
<td>0 (0%)</td>
<td>6 (100%)</td>
<td>6</td>
</tr>
<tr>
<td>6 - &lt;12</td>
<td>30 (25%)</td>
<td>89 (75%)</td>
<td>119</td>
</tr>
<tr>
<td>12 - &lt;18</td>
<td>144 (23%)</td>
<td>480 (77%)</td>
<td>624</td>
</tr>
<tr>
<td>Total</td>
<td>174 (23%)</td>
<td>575 (77%)</td>
<td>749</td>
</tr>
<tr>
<td>Age (Yr)</td>
<td>No (n, %)</td>
<td>Yes (n, %)</td>
<td>Total</td>
</tr>
<tr>
<td>----------</td>
<td>-----------</td>
<td>------------</td>
<td>-------</td>
</tr>
<tr>
<td>&lt;2</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0</td>
</tr>
<tr>
<td>2 - &lt;6</td>
<td>6 (50%)</td>
<td>6 (50%)</td>
<td>12</td>
</tr>
<tr>
<td>6 - &lt;12</td>
<td>42 (45%)</td>
<td>51 (55%)</td>
<td>93</td>
</tr>
<tr>
<td>12 - &lt;18</td>
<td>174 (45%)</td>
<td>209 (55%)</td>
<td>383</td>
</tr>
<tr>
<td>Total</td>
<td>222 (45%)</td>
<td>266 (55%)</td>
<td>488</td>
</tr>
</tbody>
</table>
Conclusions

- ~80% of pediatric IBD patients are 12 to 17 years of age
  - ~20% age 6 to 11 years
  - <6 years is rare
- CD to UC ratio is 2.5:1
- Many patients have moderate-severe disease activity at some point in their disease course
  - ~70% - 80% of patients in clinical remission at any given time
  - ~5% - 10% have moderate to severe disease activity
- ~50% patients IM experienced; 50% biologic experienced
- Persistence on 1st anti-TNF for CD: 74% at 3 years
  - Somewhat lower for UC
- Large, multicenter registry can be used to estimate number of patients who may meet inclusion/exclusion criteria for a trial
Race and ethnicity (patients < 18 at time of registration)

<table>
<thead>
<tr>
<th>Race</th>
<th>CD (n=21,150)</th>
<th>UC (n=9,549)</th>
<th>IBD NOS (n=2,793)</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>14,761 (82%)</td>
<td>6,434 (82%)</td>
<td>1,857 (81%)</td>
</tr>
<tr>
<td>Black</td>
<td>1,991 (11%)</td>
<td>728 (9%)</td>
<td>243 (11%)</td>
</tr>
<tr>
<td>Asian</td>
<td>442 (2%)</td>
<td>249 (3%)</td>
<td>76 (3%)</td>
</tr>
<tr>
<td>Other</td>
<td>742 (4%)</td>
<td>475 (6%)</td>
<td>110 (5%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>CD (n=21,150)</th>
<th>UC (n=9,549)</th>
<th>IBD NOS (n=2,793)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latino</td>
<td>890 (6%)</td>
<td>788 (12%)</td>
<td>162 (8%)</td>
</tr>
<tr>
<td>Not Latino</td>
<td>14,026 (94%)</td>
<td>5,800 (88%)</td>
<td>1,949 (92%)</td>
</tr>
</tbody>
</table>