

# Crohn's Disease Among the Poorest Billion



Program in Global NCDs  
and Social Change  
HARVARD MEDICAL SCHOOL





# table of contents

Crohn's Project Team & Acknowledgements

List of Tables

List of Figures

Acronyms & Abbreviations

## **1 Executive Summary • 9**

1.0 Background & Context

1.1 Introduction to Crohn's Disease in LLMICs

1.2 Project Objectives

## **2 Methodology • 19**

2.1 Scoping Literature Review

2.2 Provider Survey

2.3 Site Visits

## **3 Key Findings • 27**

3.1 Burden of Crohn's Disease in LLMICs

3.2 Crohn's Diagnostic and Treatment Capacity in LLMICs

3.3 Socioeconomic Characteristics of Individuals with Crohn's in LLMICs

3.4 Challenges & Barriers to Providers and Individuals with Crohn's in LLMICs

## **4 Crohn's Disease Patient Profiles • 43**

4.1 India

4.2 Nepal

4.3 Ethiopia

## **5 Conclusions • 48**

5.1 Summary of Findings

5.2 Key recommendations

References

## **Appendix • 59**

Appendix 1.0 Scoping Review Supplemental Results

Appendix 2.0 Provider Survey Supplemental Results

Appendix 3.0 Site Visit Summaries

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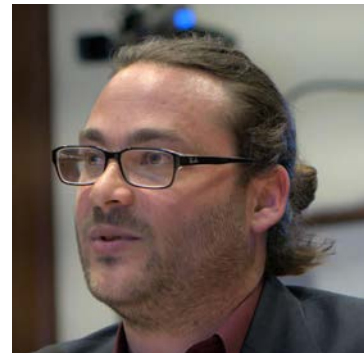
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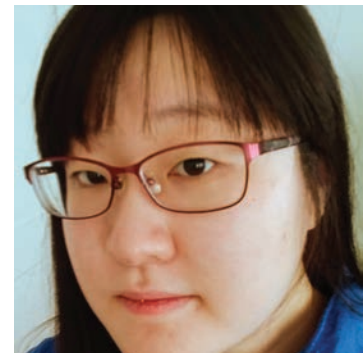
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## tables

- |                     |   |
|---------------------|---|
| <b>Table 1 • 30</b> | Mean number of cases and range of Crohn's reported by each study included in the scoping review, overall, by region, and by LLMIC   |
| <b>Table 2 • 31</b> | Mean and range number of patients reportedly diagnosed with IBD and Crohn's cared for in the last year, and percentage of IBD that is diagnosed as Crohn's, reported overall, by region, and by country |
| <b>Table 3 • 32</b> | Prevalence and incidence of IBD and CD reported by each study included in the review, by LLMIC  |
| <b>Table 4 • 34</b> | Utilization of Crohn's disease diagnostic and treatment services reported in studies included in the scoping review by region and country   |
| <b>Table 5 • 35</b> | Number of studies in the scoping review reporting Crohn's disease diagnostic and treatment services by region and country   |
| <b>Table 6 • 40</b> | Most frequently reported diagnostic, management, access, and financial challenges and barriers to Crohn's patients and providers in LLMICs as reported in the Crohn's provider survey                   |
| <b>Table 7 • 41</b> | Ranges of costs to patients of common Crohn's disease treatments as reported by survey respondents in the Crohn's provider survey   |

- Figure 1 • 22** Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram Asia site visit locations in India, Nepal, and Pakistan
- Figure 2 • 25** Asia site visit locations in India, Nepal, and Pakistan
- Figure 3 • 26** Africa site visit locations in Rwanda, Malawi, and Ethiopia
- Figure 4 • 29** LLMICs with and without published Crohn’s disease studies; summary of studies in the scoping review describing Crohn’s disease case by world region and LLMIC
- Figure 5 • 31** Mean number of Crohn’s patients cared for in the last year, by LLMIC as reported in the Crohn’s provider survey
- Figure 6 • 32** Number of survey respondents from each LLMIC included in the analysis; Number of gastroenterologists and endoscopy centers in each country as reported by survey respondents
- Figure 7 • 36** Availability of Crohn’s diagnostic technology in LLMICs as reported in the Crohn’s provider survey, overall and by region
- Figure 8 • 36** How providers in LLMICs differentiate between Crohn’s disease and intestinal tuberculosis as reported in the Crohn’s provider survey
- Figure 9 • 37** Availability of Crohn’s treatments in LLMICs, overall and by region as reported in the Crohn’s provider survey
- Figure 10 • 38** Proportion of providers who do and do not record socioeconomic characteristics of patients in the Crohn’s provider survey
- Figure 11 • 42** Challenges faced by providers in diagnosing Crohn’s disease, across all LLMICs, as reported in the Crohn’s provider survey
- Figure 12 • 42** Challenges faced by providers in managing Crohn’s disease, across all LLMICs, as reported in the Crohn’s provider survey

# acronyms & abbreviations

<b>AFB</b>	Acid-fast Bacilli
<b>AIG</b>	Asian Institute of Gastroenterology
<b>AIIMS</b>	All India Institute of Medical Sciences
<b>ATT</b>	Anti-tubercular Therapy
<b>CD</b>	Crohn's Disease
<b>CDAI</b>	Crohn's Disease Activity Index
<b>CHUK</b>	Centre Hospital University Kigali
<b>CRP</b>	C-reactive Protein
<b>CT</b>	Computed Tomography
<b>DALY</b>	Disability Adjusted Life Years
<b>DKS</b>	Dau Kalyan Singh
<b>DRC</b>	Democratic Republic of Congo
<b>ERCP</b>	Endoscopic Retrograde Cholangiopancreatography
<b>ESR</b>	Erythrocyte Sedimentation Rate
<b>EUS</b>	Endoscopic Ultrasound
<b>GBD</b>	Global Burden of Disease
<b>GI</b>	Gastrointestinal
<b>HIC</b>	High Income Country
<b>IBD-U</b>	Inflammatory Bowel Disease Unspecified
<b>IBD</b>	Inflammatory Bowel Disease
<b>IC</b>	Indeterminate Colitis
<b>ICU</b>	Intensive Care Unit
<b>IGRA</b>	Interferon Gamma Release Assay
<b>IMEMR</b>	Index Medicus for the Eastern Mediterranean Region
<b>IMSEAR</b>	Index Medicus for the South East Asia Region
<b>IRB</b>	Institutional Review Board
<b>ITB</b>	Intestinal Tuberculosis

<b>KM</b>	Kilometers
<b>LILACS</b>	Latin America and the Caribbean Literature on Health Sciences
<b>LLMIC</b>	Low- and Lower-Middle Income Country
<b>LMIC</b>	Lower Middle-Income Country
<b>MBT</b>	Mycobacterium
<b>MeSH</b>	Medical Subject Headings
<b>MG</b>	Milligram
<b>MR</b>	Magnetic Resonance
<b>MTB</b>	Mycobacterium Tuberculosis
<b>NCD</b>	Noncommunicable Diseases
<b>NCDI</b>	Noncommunicable Diseases and Injuries
<b>NGO</b>	Non-Governmental Organization
<b>NILGID</b>	National Institute of Liver and GI Diseases
<b>PCR</b>	Polymerase Chain Reaction
<b>PEG</b>	Percutaneous Endoscopic Gastronomy
<b>PRISMA</b>	Preferred Reporting Items for Systematic Reviews and Meta-analyses
<b>SES</b>	Socioeconomic Status
<b>SIUT</b>	Sindh Institute of Urology and Transplantation
<b>TB</b>	Tuberculosis
<b>TB-PCR</b>	Tuberculosis Polymerase Chain Reaction
<b>TNF</b>	Tumor Necrosis Factor
<b>TPMT</b>	Thiopurine Methyltransferase
<b>UC</b>	Ulcerative Colitis
<b>UMIC</b>	Upper-Middle Income Country
<b>USA</b>	United States of America
<b>USD</b>	United States Dollars
<b>WGO</b>	World Gastroenterology Organization
<b>WHO</b>	World Health Organization
<b>WPRIM</b>	Western Pacific Region Index Medicus



# executive summary

The objective of the Crohn's Disease Among the Poorest Billion project was to illuminate the burden of Crohn's disease in Low and Lower-Middle Income Countries, with a focus on populations living in extreme poverty.



**The Lancet Commission** on Reframing Noncommunicable Diseases and Injuries (NCDIs) for the Poorest Billion living in extreme poverty has charted an agenda to address NCDIs among the world's poorest, 90% of whom live in rural sub-Saharan Africa and South Asia. • This Commission has highlighted the **importance of disease severity** in priority setting, with an emphasis on conditions that are highly disabling or lethal among the young (those under 40 years), such as Crohn's disease.<sup>1</sup> • While over 1.5 million and 2 million people in North America and Europe, respectively, are thought to be affected by Crohn's disease,<sup>2,3</sup> the number of those suffering with Crohn's **outside the developed world is unclear** due to challenges in diagnosis, surveillance and monitoring. • There is increasing research on Crohn's in upper-middle income countries such as China<sup>4</sup>, but **there are virtually no published data on the epidemiology and care pathways for Crohn's where the Poorest Billion live.** • As epidemiologic sources from LLMICs are so limited, there is a pressing need to study the published and unpublished data on the current state of Crohn's disease in the poorest parts of the world. The objective of the Crohn's Disease Among the Poorest Billion project was to **illuminate the burden of Crohn's disease in LLMICs**, (with a focus on populations living in extreme poverty), as well as the availability of necessary diagnostic and treatment services, the characteristics of patients, and challenges and barriers to providers and patients with Crohn's disease. We carried out these objectives through the following multi-pronged approach: **① A scoping literature review ② A survey of gastroenterology providers in LLMICs and ③ Site visits to endoscopy centers in sub-Saharan African and South Asia.** We summarize our findings on the following pages.

While Crohn's disease has been studied extensively in high-income countries, its epidemiology and care in LLMICs is not well established.

Of all **79** LLMICs, only 21 (26.6%) have publications describing individuals with Crohn's disease.

Afghanistan  
Angola  
Bangladesh  
Benin  
Bhutan  
Bolivia  
Burkina Faso  
Burundi  
Cabo Verde  
Cambodia  
Cameroon  
Central African Republic  
Chad  
Comoros  
Côte d'Ivoire  
Democratic People's Republic of Korea  
Djibouti  
Egypt  
El Salvador  
Eritrea  
Ethiopia  
Gambia  
Georgia Republic  
Ghana  
Guinea Bissau  
Haiti

Honduras  
India  
Indonesia  
Kenya  
Kiribati  
Kosovo  
Kyrgyz Republic  
Lao People's Democratic Republic  
Lesotho  
Liberia  
Madagascar  
Malawi  
Mali  
Mauritania  
Micronesia  
Moldova  
Mongolia  
Morocco  
Mozambique  
Myanmar  
Nepal  
Nicaragua  
Niger  
Nigeria  
Pakistan  
Papua New Guinea

Philippines  
Republic of Congo  
Rwanda  
São Tome and Principe  
Senegal  
Sierra Leone  
Solomon Islands  
Somalia  
South Sudan  
Sri Lanka  
Sudan  
Swaziland  
Syrian Arab Republic  
Tajikistan  
Tanzania  
Timor-Leste  
Togo  
Tunisia  
Uganda  
Ukraine  
Uzbekistan  
Vanuatu  
Vietnam  
West Bank and Gaza  
Yemen  
Zambia  
Zimbabwe

Based on our provider survey, there appears to be more Crohn's disease in LLMICs than is indicated in the literature.

## Burden of Crohn's Disease in LLMICs

OUR SCOPING REVIEW yielded 216 publications which were determined to be relevant to the research questions. *Of all 79 LLMICs, only 21 (26.6%) have publications describing individuals with Crohn's disease.* Overall, most studies came from India (49.5%), followed by Tunisia (19.0%), and Egypt (8.3%). Most (73.4%) of the LLMICs do not have any studies describing individuals with Crohn's disease identified through our search (**Figure 4**).

THERE IS AN *even more severe lack of population-based epidemiologic data about Crohn's disease in LLMICs, with only four LLMICs reporting any incidence or prevalence data—India, Indonesia, Sri Lanka, and the Philippines—all of which are in Asia.*

OVERALL, the mean number of cases of Crohn's disease reported per study is 57.84 and the median is 22, but ranges widely from single-patient case studies to cohorts of as many as 980 individuals with Crohn's, and varies from country to country (**Table 1**). Countries in South Asia (63.42%) and the Middle East and North Africa (61.73%) regions reported substantially higher mean numbers of Crohn's cases per study compared to sub-Saharan Africa (3.25%) and East Asia & Pacific (2.67%).

WE CONDUCTED *a cross-sectional survey of gastroenterology providers in countries where the Poorest Billion live to determine the state of diagnostic and treatment capacity for Crohn's in the 79 identified LLMICs.* Of the 80 providers and were sent the survey link, a total of 46 (54.8%) survey responses from 15 countries were included in this analysis. The most highly represented LLMIC is India (21.7%), followed by Ethiopia (17.4%), Nepal (13.0%), Egypt (8.7%), and Nigeria (6.5%) (**Appendix 2.1**). The 46 participants who took the survey represent 33

health facilities across the 15 LLMICs, with only three (9.4%) located in rural areas.

OVERALL, *the mean number of patients diagnosed with Crohn's cared for in the last year by survey respondents, was 89.5 and varied widely from 0 reported at one facility in Rwanda, to 1,000 reported at two different facilities in India (Table 2).* Besides the facilities in India, two facilities in Bangladesh and Nepal reported the next highest number of Crohn's disease patients in Asia at 60 and 40 respectively. In Africa, the highest numbers of Crohn's disease patients were reported from facilities in Ethiopia and Tunisia at 130 and 90, respectively. *Overall, Crohn's disease made up 20.6% of the IBD diagnoses reported by survey respondents. This percentage also varied between countries and regions, with Africa having a larger proportion of Crohn's (43.4%) compared to UC than Asia (19.2%).*

THERE APPEARS *to be more Crohn's disease in LLMICs than is indicated in the literature. This is particularly true for Ethiopia, which has virtually no published IBD data but is seeing increasing patients being diagnosed with IBD and one of the highest proportions of Crohn's (69.4%) compared to UC of the included countries.* This discrepancy between published and unpublished Crohn's data is also the case for Nepal, where the highest number of Crohn's patients reported in any published study was 10 but, according to our provider survey, there were facilities which had taken care of up to 40 Crohn's patients in the past year. This gap in research and reporting might be reflective of providers' lack of resources and incentives for publishing data, rather than a true absence of Crohn's disease in these populations. In addition, health management information systems in these countries may not be reliable or may not require routine reporting or surveillance of Crohn's disease.

IT IS CRITICAL *to study and publish data on Crohn's disease in LLMICs, even if they are facility-based or case studies, and to set up clinical data registries so that population-based epidemiologic research can shed light on the true burden of Crohn's disease in these settings. This is particularly important in those countries where it has not been studied at all, and in rural areas, where access to appropriate health care can be an issue.*

## **Crohn's Diagnostic and Treatment Capacity in LLMICs**

OF THE 21 LLMICS included in our scoping review, all but Bolivia and Syria had at least one study discussing the utilization of Crohn's diagnostic services: blood testing, stool testing, TB testing, radiology/imaging, endoscopy, and pathology services. Of the 21 LLMICs included, all but Bolivia, Ghana, and Syria had at least one study discussing the utilization of one or more Crohn's medications or surgical treatments (**Table 4**). *Corticosteroids, aminosalicicylates, and immunomodulators are the most frequently reported medications overall, while biologic agents are the least available (Appendix 1.4). It should be noted that all of the studies in our scoping review, except one from a community hospital in Bolivia, were from large tertiary referral or specialty hospitals, associated with a university or the military. Thus, the availability of these diagnostic tests at these tertiary referral facilities may not necessarily reflect the general standard of care across these countries; they likely reflect the research environment at these institutions.*

ALL OR MOST of the providers surveyed reported having access to basic Crohn's diagnostic testing such as tissue pathology, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), TB testing modalities, upper endoscopy, colonoscopy, X-ray, barium enema, small-bowel follow-through, and abdominal CT scans (**Figure 7**). Of note, stool calprotectin was widely available to respondents from Asian LLMICs but was only available to half of providers from Africa. First line Crohn's

medications, such as Prednisolone, Mesalamine, Sulfasalazine, and Azathioprine, are widely reported to be available by providers across all of the included LLMICs (**Figure 9**). The two most critical IBD surgeries, colectomy and small bowel resection, are also commonly available to the providers surveyed (**Appendix 2.6**). *The availability of more advanced surgeries and alternative medications are much more variable across world regions and from country to country. Biologic agents such as Infliximab and Adalimumab were reportedly available to most providers in Asia (76.2%), compared to only 31.8% of respondents from Africa.*

MOST OF *the providers reported that patients with Crohn's have symptoms for between 6 and 24 months prior to diagnosis.* Five providers from India, Ethiopia, Nepal, Nigeria, and Zimbabwe reported that their patients typically have symptoms for more than 24 months (**Appendix table 2.3**).

IN ORDER TO BETTER UNDERSTAND the state of Crohn's disease in LLMICs, we also carried out site visits to a total of 20 hospitals with endoscopy facilities in India, Nepal, Pakistan, Malawi, Ethiopia, and Rwanda. Most of the hospitals we visited in both Asia and Africa were large tertiary facilities in urban centers and thus had many of the facilities necessary for diagnosing Crohn's disease. Every hospital we visited in Asia and all but one in Africa (Neno District Hospital in Malawi) had endoscopy and colonoscopy facilities. Most hospitals in Asia had access to necessary radiology such as small bowel follow-through and abdominal CT. Radiology was more limited in the African countries we visited—none of the African hospitals had MR or CT enterography in their facility. Stool calprotectin was available at most of the hospitals in India but rarely carried out due to very high cost, and in Nepal, it was only available at private pathology facilities. Stool calprotectin was not available in the African hospitals we visited. TB-PCR was also available at all facilities, but was not widely used

or trusted due to high rates of false positives as a result of contamination. Most facilities we visited in Asia had access to basic IBD medications such as aminosalicylates, steroids, and immunomodulators. Most facilities in India additionally had access to biologics such as Infliximab and Adalimumab and their biosimilars, but these medications are cost prohibitive to the vast majority of patients and also increase the risk of TB reactivation, so they are not widely used. Biologics are not approved in Nepal and thus can only be imported from India, making them even more expensive and inaccessible to patients. *In Africa, most facilities had access to basic steroids such as Prednisone and immunomodulators such as Methotrexate, but were very limited in all other drug categories (Figure 9).*

## Socioeconomic Characteristics of Individuals with Crohn's in LLMICs

OF THE 216 STUDIES in 21 countries included in this review, only 29 studies in 11 countries discussed patient geographic, socioeconomic, or cost information. See **Appendix 1.5** for a summary of patient geographic residency, socioeconomic characteristics, insurance coverage, and out of pocket costs.

ALL EIGHT<sup>5-12</sup> of the studies from India that discussed patients' geography reported that more individuals with Crohn's resided in urban areas compared to rural areas (**Appendix 1.5**). Similarly, studies from Egypt<sup>13</sup>, Ethiopia<sup>14</sup>, and Indonesia<sup>15</sup> report individuals with Crohn's coming from cities more frequently. Sri Lanka, on the other hand, has a recent study reporting more cases among rural communities (73.9%) than urban (26.1%).<sup>16</sup> Two older studies from Bolivia in 1975<sup>17</sup> and Kenya in 1980<sup>18</sup> also describe more rural Crohn's patients than urban.

ONLY EIGHT studies from three of the included countries reported on socioeconomic characteristics, either income level, education

level, or employment status: India, Tunisia, and Sudan (**Appendix 1.5**). Three of the included studies from India and two from Nigeria describe out of pocket costs and insurance coverage of individuals with Crohn's Disease (**Appendix 1.5**). For example, a recent 2019 study from India reports that 14.3% of patients discontinued Adalimumab due to high cost.<sup>30</sup>

IN CONTRAST, *most of the survey participants overall estimated that approximately 26-50% of their patients diagnosed with Crohn's live in rural areas (Figure 11).* When stratified by region, Asian providers reported somewhat higher proportions of their patients living in rural areas. These numbers may be even higher given the lack of access to diagnostics in most rural areas, with patients having to travel long distances to urban centers for a diagnosis of Crohn's disease.

COLONOSCOPY with biopsy and upper endoscopy with biopsy in both Asia and Africa were reported by the most providers for a cost range less than US \$50 (**Appendix 2.8**). Abdominal CT scans are more costly to patients, with most falling in the US \$50-100 range, and one provider in Malawi reporting it costing more than US \$500 (**Appendix 2.8**). Overall, the most frequently reported cost of a hospitalization for a Crohn's disease flare was between US \$101 and \$500 (39.5%) (**Table 7**). One provider in Pakistan reported that being hospitalized for a Crohn's flare could cost a patient over US \$5,000 (**Appendix 2.9**). The most frequently reported cost of biologics overall is over US \$500 (32.6%), followed closely by the US \$100-500 category (27.9%) (**Appendix 2.9**). It should be noted there is a substantial amount of missing data for the cost-related survey questions. In addition, these costs should be seen in the light of total health expenditure per capita of \$44 in low-income countries and \$80 in lower-middle income countries.

## Challenges & Barriers to Providers and Individuals with Crohn's in LLMICs

IN OUR SCOPING REVIEW, *the most commonly reported provider challenge is differentiating between Crohn's and intestinal tuberculosis (ITB), due to the high prevalence of TB in LLMICs and its overlap of symptoms and endoscopic features (Figure 8).* This can result in long delays in disease diagnosis and thus appropriate treatment.

THIS WAS FOLLOWED by diagnostic delays due to perceived rarity of IBD and lack of clinical awareness among providers, which was mentioned in 17 studies from eight countries, and lack of quality diagnostic facilities, which was mentioned in 14 studies from eight countries.

THE MOST FREQUENTLY *reported patient barrier was cost of Crohn's surgeries and medications.* Patients' inability to afford the costs of their treatment in general was mentioned in nine studies, and high cost of biologics specifically in three studies (Appendix 1.5).

IN OUR PROVIDER SURVEY, the most commonly reported challenge in diagnosing Crohn's disease overall is differentiating between Crohn's and ITB, particularly in Asian countries where it was reported by 79.5% of providers (Appendix 2.5). Distinguishing between Crohn's and other infectious diseases was also a frequently reported challenge in both Asia (57.1%) and Africa (52.2%), as well as patients' inability to afford the cost of diagnostic testing (52.4% in Asia and 60.9% in Africa) (Figure 12). *Gastroenterologists in Africa particularly struggle with poor Crohn's disease awareness among providers (47.7%) and lack of trained pathologists (36.4%) in accurately diagnosing Crohn's (Figure 12).*

IN OUR PROVIDER SURVEY, the most widely reported challenge in managing Crohn's disease overall is patients' inability to afford biologics, particularly in African countries where it was reported by 72.7% of providers (Appendix 2.7). Lack of access to biologics is also a major challenge for African gastroenterologists (68.2%), as is patients' inability to afford other treatments (50.0%).



## patient stories

In 2019, we visited a total of **14** endoscopy facilities in Asia: **six** in India, **five** in Nepal, and **three** in Pakistan. We also visited **five** endoscopy facilities in **three** countries in sub-Saharan Africa: **one** in Malawi, **three** in Ethiopia, and **one** in Rwanda.

facilities were visited

*While visiting AIG's IBD clinic, we had the chance to talk to a young Crohn's patient and her mother. The patient was a **14-year-old girl**, who was diagnosed with Crohn's in March 2017 at the age of 12. When M was diagnosed, she was malnourished due to severe vomiting and diarrhea. She would significantly benefit from biologic therapy, but she cannot receive it due to her family's inability to afford the treatment.*

*At Nidan Hospital, we had the chance to speak with one of Dr. Neeraj Joshi's long-time Crohn's disease patients, a **50-year-old man** named S. He was diagnosed with Crohn's 20 years ago due to a bowel obstruction, 4-5 years after having surgery for a burst appendix. S noted he feels dependent on steroids and wonders if he can be weaned off the steroid and start an alternative treatment.*

*The most impactful patient we have met was a **medical intern** at Saint Paul's Hospital, who was recently diagnosed with Crohn's disease while she was in medical school. The diagnosis took eight months to confirm, and during a very severe flare she considered quitting school as her professors didn't understand her need for time off.*



# 1.0 background & context

## 1.1 Introduction to Crohn's Disease in LLMICs

CROHN'S DISEASE (CD) is a chronic gastrointestinal disease typically characterized by inflammation of the terminal ileum and colon resulting in abdominal pain, severe diarrhea, and other debilitating symptoms<sup>23</sup>, as well as complications such as fistulas and strictures, ultimately requiring surgery in many cases. CD appears to be only moderately heritable<sup>22</sup>, and multiple possible environmental and behavioral causes have been invoked<sup>23</sup>, including insufficient contact with infectious diseases in childhood (the hygiene hypothesis), antibiotic exposure, tobacco use, and consumption of highly processed foods. CD has historically been regarded as a "lifestyle" disease of industrialized countries.<sup>24,25</sup> First described in the United States in 1932, CD was increasingly diagnosed in Europe and North America during the 20th century, where around 0.5% of the population is now thought to be affected.<sup>26</sup> More recently, CD has been recognized in the rapidly developing upper-middle income countries of East Asia<sup>27</sup> and South America,<sup>28</sup> with prevalence rates as high as 24 per 100,000 in Brazil,<sup>29</sup> and 11 per 100,000 in South Korea.<sup>30</sup>

IN CONTRAST, previous systematic reviews of the published literature on CD epidemiology have found few studies on either the prevalence or incidence of CD coming from the low- and lower-middle income countries (LLMICs). A review of population-based studies that were published between 1990 and 2016 found data from only four LLMICs. These LLMIC studies were all in Asia (the Gampaha district of Sri Lanka, the Hyderabad district of India, Manila city in the Philippines, and Central Jakarta in Indonesia), had all come out of the prospective Asia-Pacific Crohn's and Colitis Epidemiologic Study (ACCESS),<sup>31</sup> and were all focused on urban areas. All of the

countries involved in these studies are currently classified as upper-middle income by the World Bank, with the exception of India.<sup>32</sup> An earlier systematic review of incidence and prevalence studies (both population and facility-based) published between 1950 and 2010 only identified data from three countries that were classified as LLMICs at the time the research was conducted (**Appendix 1.3**). These countries were Sri Lanka (prospective study of Columbo and Gampaha districts),<sup>33</sup> Panama (retrospective review of hospital data from the Colon district),<sup>34</sup> and China (review of published reports from all hospitals). Currently, all of these countries are classified as upper-middle income. As a result, the 2017 Global Burden of Disease study largely based its CD rate estimates for LLMICs on global trends.<sup>35,36</sup>

THE VAST MAJORITY of the world's Poorest Billion people live in the rural areas of LLMICs in sub-Saharan Africa and South Asia.<sup>37</sup> In the absence of primary population data regarding CD in these countries, there has been a perception that the burden of CD remains low among the global poor. Prior systematic reviews on CD have been limited, however, by narrow inclusion criteria focused on epidemiology (incidence and prevalence). Furthermore, the lack of reports regarding CD in LLMICs may be due to limitations in access to diagnosis and treatment for CD rather than the absence of disease. The correct diagnosis of CD requires a whole chain of events beginning with patients seeking care and ending with colonoscopy and histology. A break in any part of this chain resulting from gaps in financing, education, equipment, or supplies on the part of the patient or provider can result in a missed diagnosis. Even the pathological diagnosis of CD may be confused with intestinal tuberculosis in the absence of diagnostic testing and experienced healthworkers.<sup>38,39,40</sup> CD may also have an impact on patients living in extreme

poverty that is out of proportion with the disease prevalence. Follow-up care for CD, like many other chronic diseases, requires frequent visits to health facilities, a steady supply of medications (including biologics), and often surgery. The absence of these services could result in high rates of disability and death among the poor affected by CD in LLMICs.

AS DISEASE BURDEN DATA from LLMICs are so limited, there is a pressing need to study the published and unpublished data on the current state of Crohn's disease in the poorest parts of the world. Much can be learned about a disease by studying it where it is emerging, and we feel this is a prime opportunity to study the burden and care pathways of

IBD in LLMICs. Understanding the state of Crohn's disease in LLMICs is also crucial because of the high costs to patients and to the health system to diagnose and treat even a small number of patients. For these reasons, a survey of gastroenterology providers in LLMICs is necessary to obtain a more complete view of how Crohn's impacts the Poorest Billion living in extreme poverty. The objective of this study is to expansively identify and describe the burden and care pathways of Crohn's disease in LLMICs, as well as the availability of necessary diagnostic and management services, challenges and barriers to patients diagnosed with Crohn's and providers, and the characteristics of patients diagnosed with Crohn's in LLMICs. ■

## 1.2 project objectives

The objective of the Crohn's Disease Among the Poorest Billion project is to expansively identify and describe the burden and care pathways of Crohn's disease in LLMICs, as well as the availability of necessary diagnostic and management services, challenges and barriers to providers and individuals with Crohn's, and the characteristics of patients diagnosed with Crohn's in LLMICs.

To review published literature on the epidemiology and care pathways of Crohn's disease among the world's poorest billion through a scoping literature review focused on LLMICs.

To survey gastroenterology specialists in LLMICs about the Crohn's disease burden and the state of diagnostic and treatment capacity for Crohn's in their countries.

To conduct site visits to endoscopy centers in sub-Saharan Africa and South Asia to document availability and quality of necessary Crohn's care resources, as well as carry out qualitative interviews with providers.

# methodology

Our multi-pronged approach to the research question consisted of a scoping literature review, a cross-sectional survey of gastroenterology providers in LLMICs and site visits to endoscopy centers in sub-Saharan African and South Asia.



We conducted a scoping review utilizing a full search strategy in PubMed, Embase and WHO Global Index Medicus. Two independent reviewers screened the titles and abstracts.

The provider survey consisted of 8 sections and **75** questions covering a range of clinical and demographic variables related to Crohn's disease.

Site visits were carried out to 20 hospitals in 6 countries in South Asia and sub-Saharan Africa, documenting availability and quality of necessary Crohn's care resources through qualitative interviews with gastroenterology providers.

## 2.1 scoping literature review

### Inclusion criteria

THIS REVIEW considered studies that describe cases of individuals with Crohn's disease in an LLMIC as defined by The World Bank.<sup>41</sup> The World Bank categorizes the world's countries into four income groups based on gross national income per capita: low-income countries (LIC), lower-middle income countries (LMIC), upper-middle income countries (UMIC), and high-income countries (HIC). The group of interest, low and lower-middle income countries (LLMIC), includes both LICs and LMICs, or countries with a gross national income per capita of US \$3,895 or less. To capture possible undiagnosed or misdiagnosed cases of Crohn's in LLMICs that do not have any published Crohn's data, as well as to understand their diagnostic and treatment capacity for Crohn's, studies that mention the use of diagnostics (i.e. colonoscopy, small bowel follow-through, stool calprotectin), findings (i.e. skip lesions, cobblestone, small bowel obstruction), and treatments (i.e. colectomy, small bowel resection, infliximab) utilized in managing Crohn's disease were also included. See (Appendix 1.1) for a full list of search terms. Publications that do not describe cases of individuals diagnosed with Crohn's disease were excluded from this review. Relevant secondary sources (i.e., reviews, editorials, and commentaries) were excluded and used as background information. Studies that are based on cases of Crohn's in middle, upper-middle, or high-income countries were excluded. Studies that are published in a language other than English were excluded. Studies describing non-human animals were excluded.

### Search strategy

THE SEARCH STRATEGY aimed to locate both published and unpublished studies. An initial limited search of PubMed was undertaken to identify articles on the topic. The text words contained in the titles and abstracts of relevant articles, and the index terms

used to describe the articles, were used to develop a full search strategy for PubMed in collaboration with an experienced medical librarian (Appendix 1.1). The search strategy, including all identified keywords and index terms, was adapted for Embase and WHO Global Index Medicus. The team used free text and Medical Subject Headings (MeSH), when applicable. Searches were conducted on publications in English for all years.

### Information sources

THE INFORMATION SOURCES for this review were the databases PubMed, Embase, and WHO Global Index Medicus, which includes AMRO (Africa), IMEMR (Eastern Mediterranean), IMSEAR (South East Asia), LILACS (Americas), and WPRIM (Western Pacific), as well as MEDLINE and SciELO. Authors of papers were contacted in instances where additional data was unavailable.

### Study selection

FOLLOWING THE SEARCH on May 14, 2019, all identified citations were collated and uploaded into EndNote X9 2018 (Clarivate Analytics, PA, USA) and duplicates were removed. The study selection process consisted of two parts. First, two independent reviewers (SB & SM) screened the title and abstracts of all of the initially selected publications and included all of the studies that indicated a signal of Crohn's disease, IBD, or any related Crohn's diagnostics or Crohn's treatment in an LLMIC. Studies that met or could potentially meet the inclusion criteria were saved for full text review in EndNote. Any disagreements that arose between the reviewers were resolved through discussion, or with a third reviewer (RR).

NEXT, A FULL TEXT REVIEW was conducted to categorize the studies based on country and relevance to the research question. Two independent reviewers

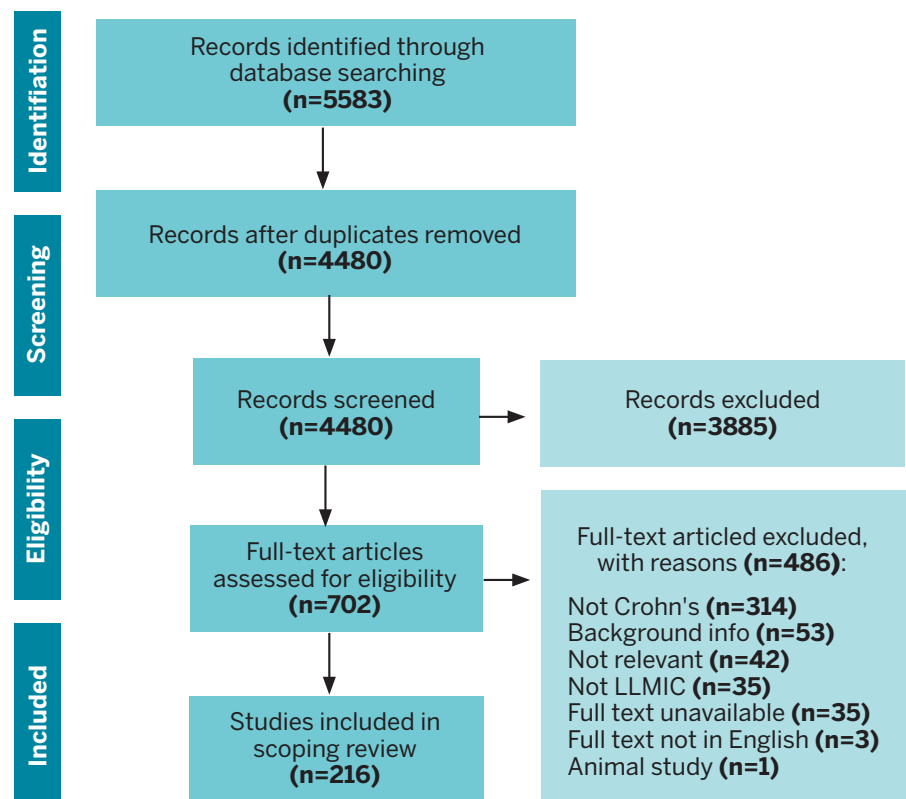
(KN & SM) assessed the full text of selected citations in detail against the inclusion criteria. Reasons for exclusion of full text studies that did not meet the inclusion criteria were recorded and are reported in the appendix. The results of the search are reported in full in the final scoping review and presented in a Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram (**Figure 1**). Any disagreements that arose between the reviewers were resolved through discussion, or with a third reviewer (SB).

## Data extraction

FULL TEXT of the publications selected were reviewed by two independent researchers and data was extracted using a pre-structured and tested data collection form in Microsoft Excel. The data extracted includes specific details about the state of Crohn's disease burden and care in LLMICs according to the review questions and specific objectives of the study. Any disagreements that arose between the reviewers were resolved through discussion, or with a third reviewer. Authors of papers were contacted to request missing or additional data, where required. A charting table was developed (**Appendix 1.2**) to record key information of the source, including the title, author, journal, date of publication, country, study years, study design, and results relevant to the review questions. In relation to burden, we collected data on number of cases reported, prevalence, incidence, odds, mortality

rate, disability-adjusted life year (DALY) rate, and average disease duration. Patient characteristics include both sociodemographic characteristics (age, residency, socioeconomic status (SES), insurance coverage, out of pocket expenses) and clinical features of their disease (IBD type, age at diagnosis, sex, risk factors, disease severity, disease behavior, and disease location, Crohn's Disease Activity Index (CDAI), extraintestinal manifestations, comorbidities, and disease outcomes). Qualitative information about disease diagnosis, management, long-term and follow-up care, and complications was documented to understand care pathways. Availability of diagnostic and treatment services included blood tests, stool tests, tissue pathology, TB testing, endoscopy, radiology/imaging, other equipment, providers, and financing. Qualitative information about provider challenges (diagnostic and management) and patient barriers (access and financial) were collected in the table.

**Figure 1.** Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram depicting the number of studies identified and excluded at each stage of the review process.



## Data Analysis

THE DESCRIPTIVE FINDINGS extracted from the studies identified were charted to summarize the results of the research objectives of this review. The charted data then underwent a narrative review and descriptive analysis to identify emerging themes found in the data in terms of Crohn's care pathways and availability of diagnostic and treatment services. Quantitative data regarding the burden of Crohn's were analyzed in Excel.

## 2.2 provider survey

### Study Design and Data Collection

WE CONDUCTED a cross-sectional survey of gastroenterology providers in countries where the Poorest Billion live to determine the state of diagnostic and treatment capacity for Crohn's in the 79 identified LLMICs. The World Bank categorizes the world's countries into four income groups based on gross national income per capita: low-income countries (LIC), lower-middle income countries (LMIC), upper-middle income countries (UMIC), and high-income countries (HIC). The group of interest, low and lower-middle income countries (LLMIC), includes both LICs and LMICs, or countries with a gross national income per capita of US \$3,895 or less. The provider survey consists of eight sections and includes 75 questions regarding Crohn's disease frequency, patient characteristics, diagnosis, treatment, monitoring and maintenance, provider demographic characteristics, and health facility characteristics. Most questions were multiple choice, but some allowed respondents to type their answer (i.e., number of patients diagnosed with Crohn's cared for in the last year). Data collection began in March 2019 and continued through mid-December 2019. Surveys were administered online via Partners REDCap secure web platform, in person, and by phone about the availability of necessary IBD diagnostic and treatment technology and resources. These included

laboratory testing of stool and blood, endoscopy, radiography, colonoscopy, and pathology services. Availability of treatments and drugs are also included on the survey, such as anti-inflammatory agents, corticosteroids, immunomodulators, anti-TNF agents, antibiotics and probiotics, as well as capacity for surgical intervention. The survey also inquired about availability of clinical registries and the nature and quality of such registries. Our goal was to reach at least one gastroenterology leader in each of the 79 countries where the world's Poorest Billion live.

### Participant Selection and Recruitment

WE RECRUITED medical professionals who provide gastroenterology care to patients in an LLMIC to complete the study survey. Gastroenterology providers of all levels and working at any type of health facility were eligible for the study. Participation was not restricted based on age, sex, race, or any other provider characteristics.

WE RECRUITED gastroenterology providers from LLMICs at World Gastroenterology Organization's Gastro 2018 conference in Bangkok, Thailand in December 2018. The providers we met at Gastro 2018 were sent a follow-up email to confirm their willingness to participate and to ask for referrals to other gastroenterologists in their country. The remainder of the participants were recruited through referral recruitment, internet searches, and contacting gastroenterologists on LinkedIn. We reached out to providers by email and gave them the option to complete the survey online or over the phone. Those who expressed interest were either sent the survey link or scheduled for a phone interview. Participants were given a detailed fact sheet in lieu of formal written consent.

### Statistical Analysis

DESCRIPTIVE SUMMARY statistics were applied to basic data regarding provider and facility characteristics to describe the sample using counts

and percentages. Categorical data about the burden of Crohn's, care pathways, and the availability of diagnostics and treatments collected from provider surveys were analyzed using chi-square or Fisher's exact tests. Quantitative data were analyzed in R and Excel.

## 2.3 site visits

### Asia Site Visits

IN MARCH AND APRIL 2019, we visited a total of 11 endoscopy facilities in Asia, six in India and five in Nepal (**Figure 2**). We started our site visits in southern India at the Asian Institute of Gastroenterology in Hyderabad, the largest gastroenterology hospital in the world. We spent two days touring their state-of-the-art facilities and meeting with the chairman of the hospital, Dr. Nageshwar Reddy, and the director of the IBD clinic, Dr. Rupa Banerjee. Both are world renowned gastroenterologists and are innovators in their field. Next, we flew to central India in Raipur, which is the capital of the state of Chhattisgarh, where we spent one day visiting four facilities.

WE WERE SURPRISED to learn that there are no gastroenterologists in the public sector in Raipur, so surgeons perform any basic upper endoscopies and colonoscopies at public tertiary hospitals. We started by meeting Dr. Kamlesh Jain from the Department of Community Medicine at Raipur Medical College and the NCD chair for the state. He introduced us to three surgeons who perform endoscopy at Raipur Medical College. We went on to visit three private hospitals, so we could meet some of Raipur's gastroenterologists at Ram Krishna Care, DKS Postgraduate Institute, and MMI Narayana. Our last stop in India was in Delhi at All India Institute of Medical Sciences (AIIMS), a large public tertiary teaching hospital with a busy IBD clinic, where we spent two days. We met with Drs. Vineet Ahuja and Saurabh Kedia, who have a large cohort of IBD patients and have published numerous studies on IBD in India.

We then made our way to Kathmandu, where we visited two large public hospitals in the city, Institute of Medicine and Bir Hospital. We also met with gastroenterologists practicing just outside of Kathmandu in Patan, at the public Patan Hospital and private Nidan Hospital. We also had the chance to travel outside Kathmandu to the more rural area of Dhulikhel, where there is a very modern community hospital whose endoscopy suite has immense support from a German NGO. Their endoscopy setup was impressive and looked like it could have easily been an endoscopy suite in the US.

IN JULY 2019, we visited three hospitals with endoscopy facilities in Pakistan, all of which were located in the city of Karachi. We started the first site visit at the Sindh Institute of Urology and Transplantation (SIUT), which is a dialysis and kidney transplant center, and serves as Pakistan's largest public sector health care organization. There, we met with Dr. Abbas Ali Tasneem, who is a gastroenterologist and senior consultant at the facility. He gave us a quick tour of the facility and showed us that pathology and radiology services are all in the building, which he noted is convenient for quick diagnoses. The next day, we visited Dow University National Institute of Liver & GI Diseases (NILGID), which is an institute within Dow University Hospital that cares for patients with liver and gastrointestinal diseases through multidisciplinary approaches. We sat down with Dr. Muhammad Majeed, who is a gastroenterologist in the department. He talked to us a little bit about the background of the facility, and the busy environment in which they serve patients. Dr. Majeed told us about the hundreds of endoscopy and colonoscopy procedures performed at the institutions and reported that there are very few patients who actually have inflammatory bowel disease. Lastly, we visited The Indus Hospital located in the town of Korangi in Karachi. We first met with Dr. Naila Baig-Ansari, who is the chair of Indus Hospital Research Center. After we shared our IRB approval for the study as





well as the survey tools, she allowed us access to speak with one of their lead gastroenterologists and consultants, Dr. Manzoor Hussain. He took time out of his schedule to answer our questions in the research department. Like SIUT, Indus Hospital is a public hospital with free services, so most of the

patients that we happened to see on our way up to the research department were extremely poor and had traveled long distances to receive care. The endoscopy services available in all three hospitals seemed very efficient, well-staffed, and very well-kept.

## ETHIOPIA

Black Lion Hospital/WGO Training Center  
Addis Ababa

Saint Paul's Hospital  
Addis Ababa

Teklehaimanot General Hospital  
Addis Ababa

## RWANDA

University Teaching Hospital of Kigali  
(CHUK)  
Kigali

## MALAWI

Neno District Hospital  
Neno

Queen Elizabeth Central Hospital (QECH)  
Blantyre

**Figure 3.** Africa site visit locations in Rwanda, Malawi and Ethiopia

## Africa Site Visits

IN AUGUST 2019, we visited five endoscopy facilities in three countries in sub-Saharan Africa: one in Malawi, three in Ethiopia, and one in Rwanda (**Figure 3**). We started our site visits in Malawi at Queen Elizabeth Central Hospital (“Queens”), a large government hospital in the center of Blantyre. Queens is the home base of Malawi’s only gastroenterologist, an ex-pat from the UK, Dr. Peter Finch. Queens endoscopy suite also serves as the World Gastroenterology Organization’s (WGO) Malawi endoscopy training center. In addition to Dr. Finch, we also met with Dr. Patrick Noah, a surgeon who also performs endoscopy. We then spent a day at Neno District Hospital, which does not have endoscopy, but does see a fair amount of gastrointestinal conditions like upper GI bleeding and esophageal cancer that require referral to Queens for diagnostic and therapeutic endoscopy. Next, we flew to Addis Ababa, Ethiopia, for a busy day visiting three endoscopy facilities at the public

Black Lion Hospital and Saint Paul’s Hospital, and the private Teklehaimanot General Hospital. There we met with Dr. Hailemichael Desalegn Mekonnen, Dr. Rezene Behre, and Dr. Yohannes Birhanu, all of whom see Crohn’s disease in their clinical practice. While visiting Saint Paul’s Hospital, we met a Crohn’s patient who is also a medical resident, who is passionate about helping Crohn’s patients in Ethiopia and has started a Crohn’s disease support group. Finally, we flew to Kigali, Rwanda to meet with Dr. Benoit Seminega, the main gastroenterologist in the country, and Dr. Eric Rutaganda, an internal medicine specialist also practicing endoscopy at CHUK (pronounced “Shi-ash-ka”).

OF NOTE, we chose India, Nepal, Malawi, Ethiopia, and Rwanda for our site visits because they have ongoing National/State-level NCDI Poverty Commissions that are looking at expanding access to priority NCDI services for populations living in extreme poverty. ■

# key findings

Of all 79 LLMICs, only 21 (26.6%) have publications describing individuals with Crohn's disease. However, based on our provider survey, there appears to be more Crohn's disease in LLMICs than is indicated in the literature.

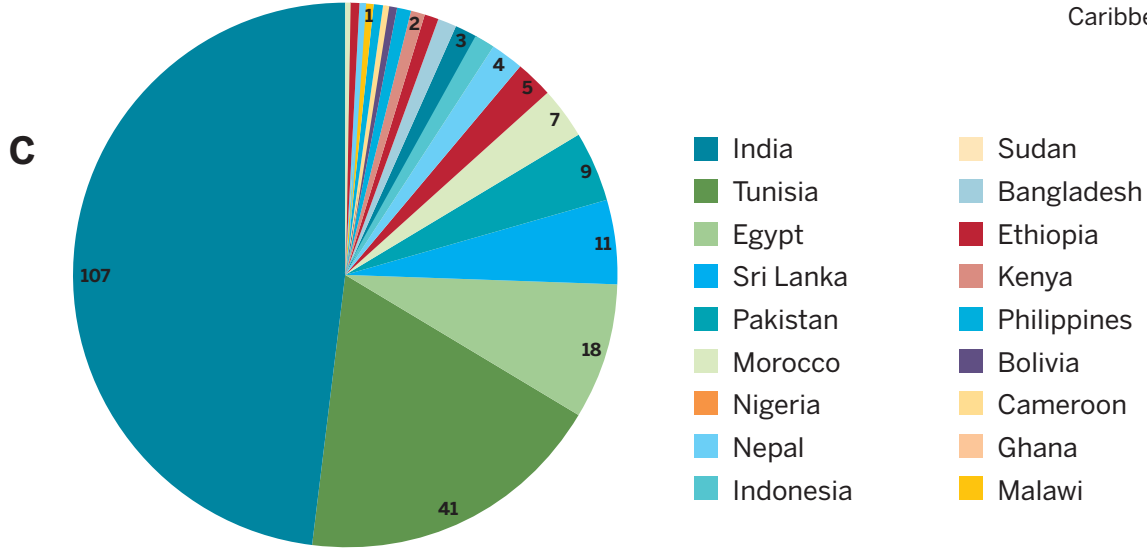
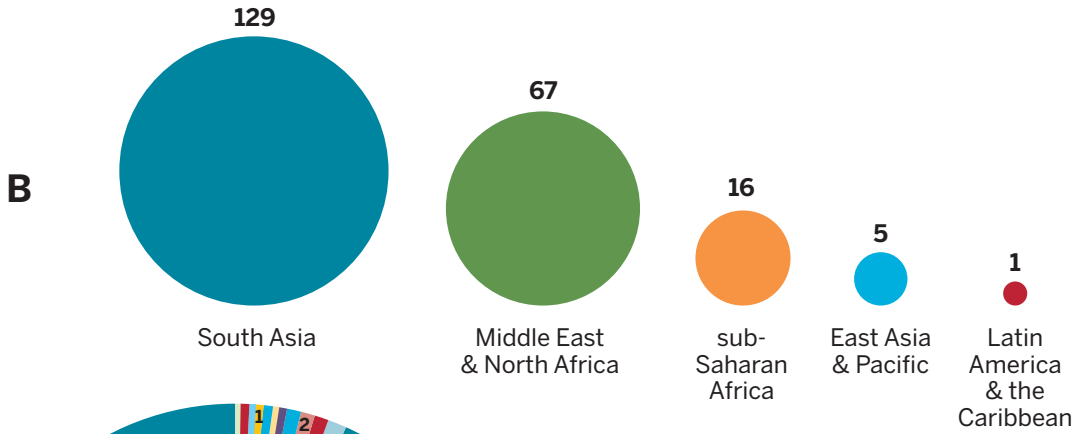
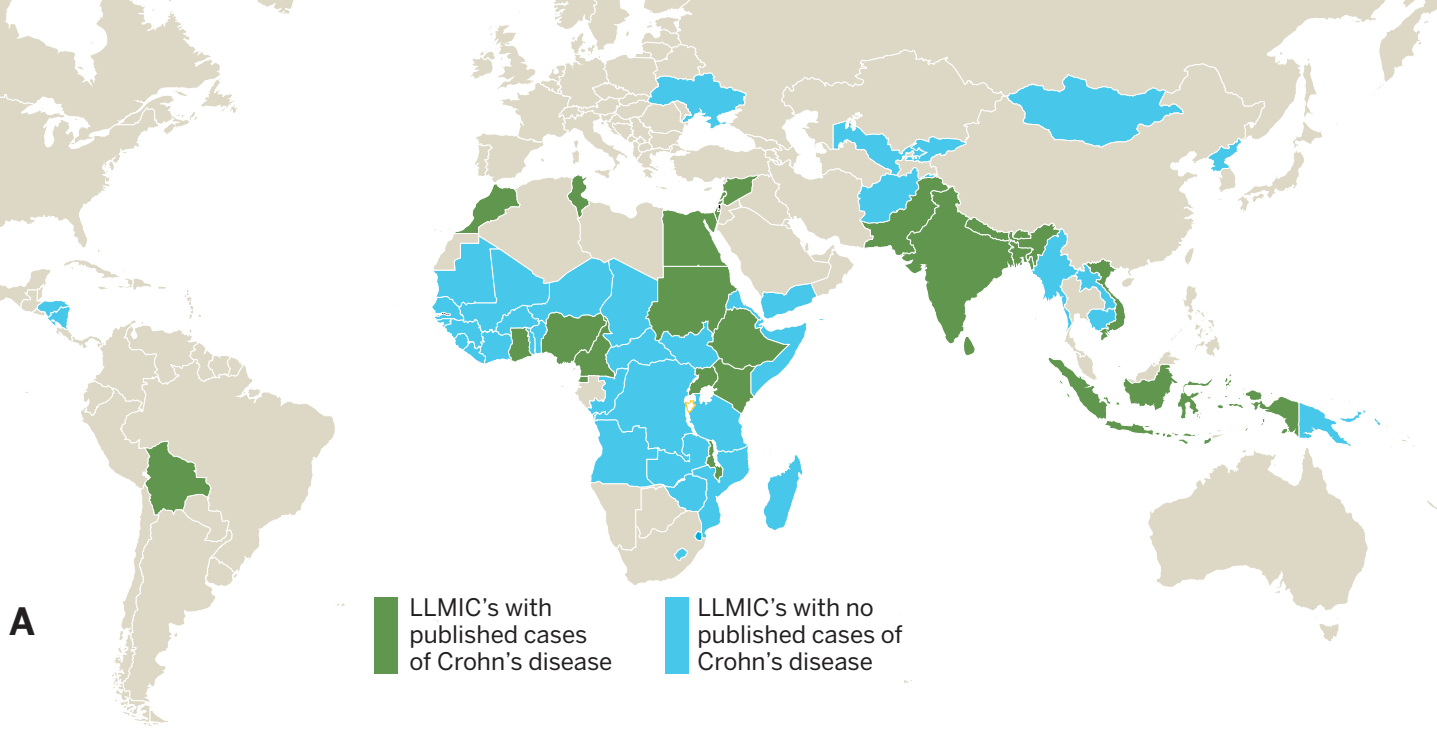


## 3.1 burden of Crohn's disease in LLMICs

The initial database search of studies that describe Crohn's disease and related diagnostics and findings in LLMICs found 4,480 publications after removing duplicates, 702 of which were kept after title and abstract screening (Figure 1). Of those 702 publications, 216 were relevant to the research questions, 208 (96.3%) of which were based in lower-middle income countries (LMICs) and 8 (3.7%) of which were based in low-income countries (Appendix 1.3 for a summary of all studies included in review by country). Of all 79 LLMICs, we only found 21 (26.6%) with studies describing individuals with Crohn's disease. Most (73.4%) of the LLMICs do not have any studies describing individuals with Crohn's disease identified through our search (Figure 4A).

Of the relevant articles, 129 (59.7%) were based in LLMICs in South Asia, 67 (31.0%) were from the Middle East and North Africa, 16 (7.4%) were from sub-Saharan Africa, 5 (2.3%) were from East Asia and Pacific, and 1 (0.5%) was from Latin America (Appendix table 1.3, Figure 4B). The majority of Crohn's studies identified are from India (49.5%), followed by Tunisia (19.0%), Egypt (8.3%), and Sri Lanka (5.1%). Bolivia, Cameroon, Ghana, Malawi, the Philippines, Syria, Uganda, and Vietnam each had one Crohn's disease study (0.5%) (Appendix 1.3, Figure 4C).

**Figure 4.** LLMICs with and without published Crohn's disease studies (A); summary of studies describing Crohn's disease cases by world region (B) and LLMIC (C).



**Table 1.** Mean number of cases and range of Crohn's reported by each study included in the review, overall, by region, and by LLMIC

Region/Country	N	Total cases	Mean	Median	Median
<b>Overall</b>	<b>220*</b>	<b>12725</b>	<b>57.84</b>	<b>22.00</b>	<b>1-980</b>
<b>South Asia</b>	<b>131</b>	<b>8485</b>	<b>64.77</b>	<b>17.00</b>	<b>1-980</b>
India	107	8054	75.27	22.00	1-980
Sri Lanka	10	332	33.20	6.00	1-153
Patistan	9	82	9.11	3.00	1-52
Nepal	4	16	4.00	2.00	1-11
Bangladesh	1	1	1.00	1.00	1
<b>Middle East &amp; North Africa</b>	<b>67</b>	<b>4165</b>	<b>62.16</b>	<b>39.00</b>	<b>1-226</b>
Tunisia	41	2984	72.78	45.00	1-226
Egypt	18	361	20.06	12.50	1-100
Morocco	7	714	102.00	101.00	68-136
Syria	1	106	106.00	106.00	106
<b>sub-Saharan Africa (N=33)</b>	<b>16</b>	<b>52</b>	<b>3.25</b>	<b>1.00</b>	<b>1-17</b>
Nigeria	5	15	3.00	1.00	1-8
Sudan	3	23	7.67	8.00	3-12
Ethiopia	2	8	4.00	4.00	1-7
Kenya	2	2	1.00	1.00	1-1
Cameroon	1	1	1.00	1.00	1
Ghana	1	1	1.00	1.00	1
Malawi	1	1	1.00	1.00	1
Uganda	1	1	1.00	1.00	1
<b>East Asia &amp; Pacific</b>	<b>5</b>	<b>15</b>	<b>3.00</b>	<b>8.00</b>	<b>1-6</b>
Indonesia	2	6	3.00	3.00	1-5
Philippines	2	3	1.50	1.50	1-2
Vietnam	1	6	6.00	6.00	6
<b>Latin America &amp; the Caribbean</b>	<b>1</b>	<b>8</b>	<b>8.00</b>	<b>8.00</b>	<b>8</b>
Bolivia	1	8	8.00	8.00	8

\*N is higher than actual number of studies due to two multi-country papers reporting cases of Crohn's

**Table 2.** Mean and range number of patients reportedly diagnosed with IBD and Crohn’s cared for in the last year, and percentage of IBD that is diagnosed as Crohn’s, reported overall, by region, and by country.

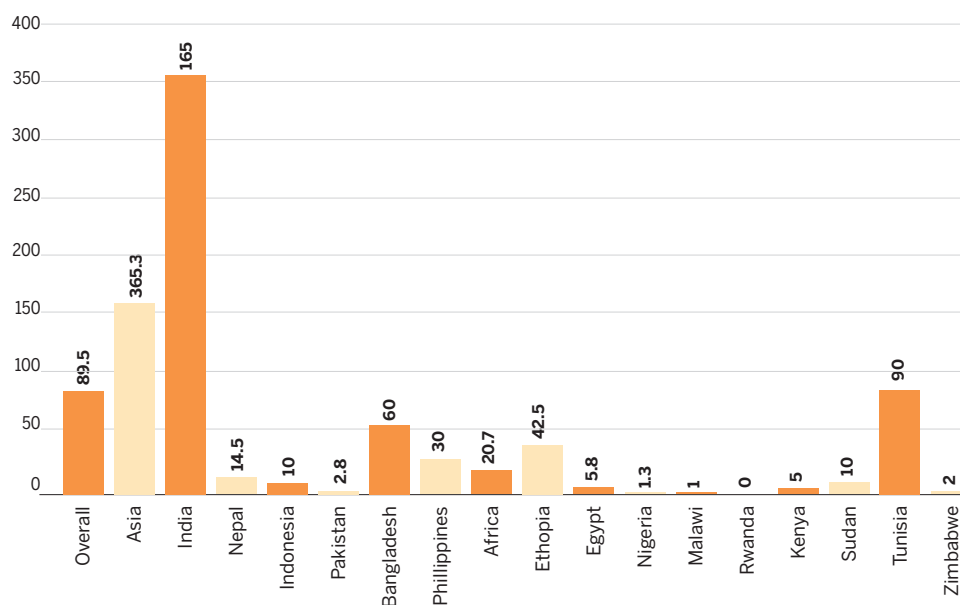
Region/Country	N	IBD*	Crohn's*	%CD
<b>Overall</b>	<b>44†</b>	<b>434.5 (0-5840)</b>	<b>89.5 (0-1000)</b>	<b>20.6</b>
<b>Asia</b>	<b>21</b>	<b>858.1 (6-5840)</b>	<b>165.0 (0-130)</b>	<b>19.2</b>
India	9†	1860.0 (20-5840)	326.3 (2-1000)	19.5
Nepal	6	129.2 (6-500)	14.5 (1-40)	11.2
Indonesia	2	120.0 (120)	10.0 (10)	8.3
Pakistan	2	32.5 (15-50)	2.8 (1-5)	8.7
Bangladesh	1	150.0 (150)	60.0 (60)	40.0
Philippines	1	50.0 (50)	30.0 (30)	60.0
<b>Africa</b>	<b>23</b>	<b>47.7 (0-150)</b>	<b>20.7 (0-130)</b>	<b>43.4</b>
Ethiopia	8	61.3 (15-150)	42.5 (5-130)	69.4
Egypt	4	86.3 (25-110)	5.8 (5-8)	6.7
Nigeria	3	5.0 (4-6)	1.3 (1-2)	26.6
Malawi	2	2.0 (0-4)	1.0 (0-2)	50.0
Rwanda	2	2.0 (2)	0 (0)	0.0
Kenya	1	100.0 (100)	5.0 (5)	5.0
Sudan	1	25.0 (25)	10.0 (10)	40.0
Tunisia	1	100.0 (100)	90.0 (90)	90.0
Zimbabwe	1	15.0 (15)	2 (2)	13.3

\*Mean (range)

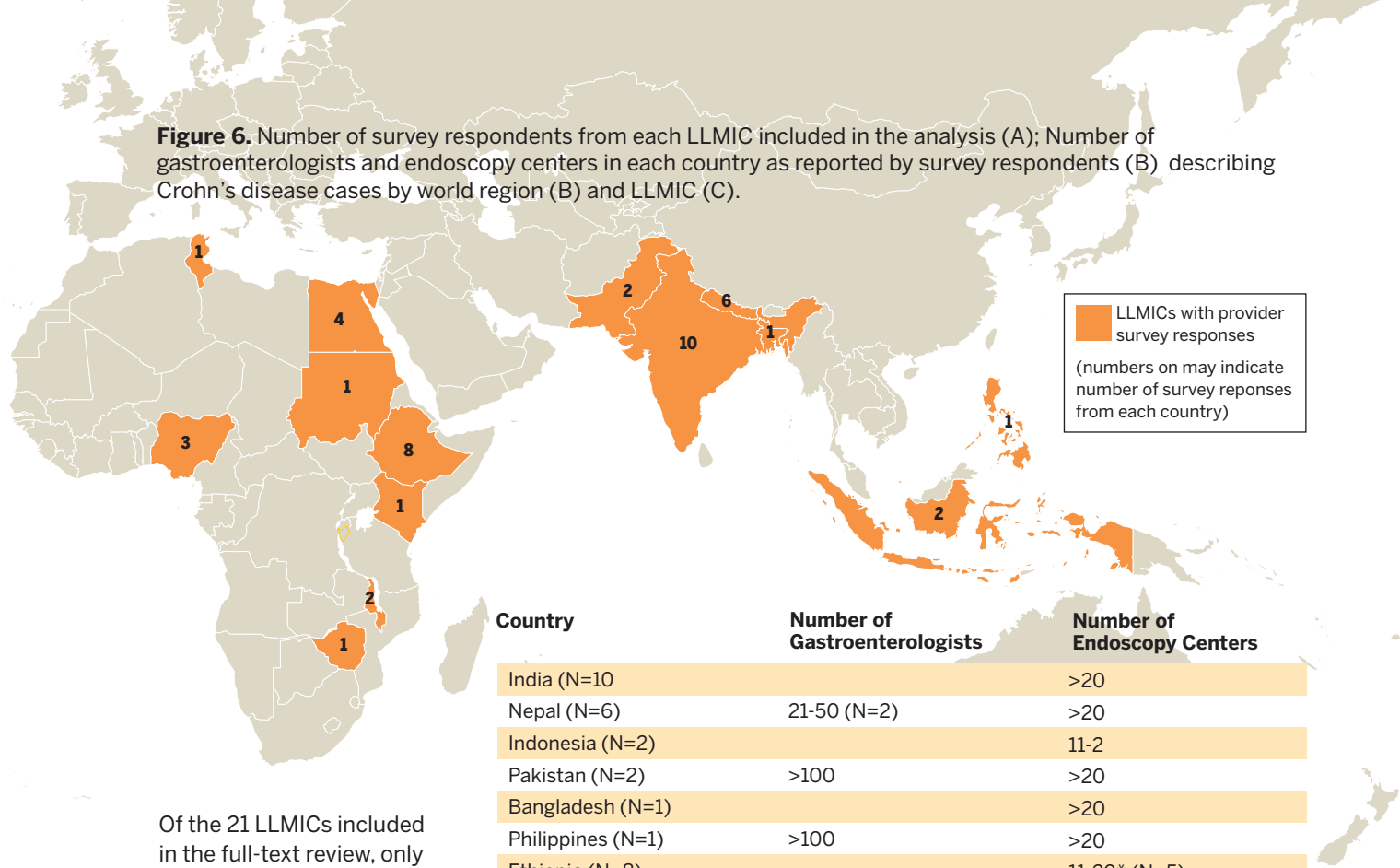
†Excludes missing data from one participant from India

Overall, 44 of the 46 providers who participated in the provider survey reported numbers of Crohn’s disease patients (Figure 5, Figure 6). The mean number of patients diagnosed with Crohn’s cared for in the last year reported was 89.5 overall and varied widely from 0 reported at one facility in Rwanda, to 1,000 reported at two different facilities in India (Figure 5, Table 2). Overall, Crohn’s disease made up 20.6% of the IBD diagnoses reported by survey respondents. This percentage also varied between countries and regions, with the Africa having a larger proportion of Crohn’s diagnoses compared to UC than Asia. These differences were most pronounced in Tunisia and Ethiopia, where providers report 90.0% and 69.4% of the mean number of IBD cases are diagnosed Crohn’s respectively, and in Indonesia, Pakistan, Egypt, and Kenya, where providers report that less than 10% of the mean number of IBD cases are diagnosed as Crohn’s.

**Figure 5.** Mean number of Crohn’s patients cared for in the last year, by LLMIC



**Figure 6.** Number of survey respondents from each LLMIC included in the analysis (A); Number of gastroenterologists and endoscopy centers in each country as reported by survey respondents (B) describing Crohn's disease cases by world region (B) and LLMIC (C).



LLMICs with provider survey responses  
(numbers on map indicate number of survey responses from each country)

Of the 21 LLMICs included in the full-text review, only two countries had studies estimating prevalence of Crohn's, India and Sri Lanka (**Table 3**). Two studies reported prevalence of Crohn's in Sri Lanka, ranging from 1.2 per 100,000 in the Colombo and Gampaha Districts in 201033, to 2.33 per 100,000 in the Central Province in 201842. Four of the 21 included countries—India, Indonesia, Sri Lanka, and the Philippines—reported incidence of Crohn's disease, with most of these data coming from one multi-country study published in 2019. This study reported annual incidence of Crohn's ranging from 0.14 per 100,000 in the Philippines to 3.91 per 100,000 in India. The 2010 study from Sri Lanka reported an annual incidence of Crohn's disease of 0.09 per 100,000 in the Colombo and Gampaha Districts.

Country	Number of Gastroenterologists	Number of Endoscopy Centers
India (N=10)		>20
Nepal (N=6)	21-50 (N=2)	>20
Indonesia (N=2)		11-2
Pakistan (N=2)	>100	>20
Bangladesh (N=1)		>20
Philippines (N=1)	>100	>20
Ethiopia (N=8)		11-20* (N=5)
Egypt (N=4)	>100	>20
Malawi (N=2)		2-10†
Nigeria (N=3)	51-100	>20
Rwanda (N=2)		6-10
Kenya (N=1)	2-5	>20
Sudan (N=2)		11-20
Tunisia (N=1)	>100	>20
Zimbabwe (N=1)		6-10

\*Indicates discrepancies in response from same country — most frequent answer presented  
†Indicates discrepancies in response from same country — ranges expanded to include consecutive categories with equal frequencies

**Table 3.** Prevalence and incidence of Crohn's disease reported by each study included in the review, by LLMIC

Country	Prevalence	
India	—	3.91 per 1000,000 [Ng, et al., 2019]
Sri Lanka	1.2 per 100,000 [Niriella et al 2010]	0.52 per 100,000 [Ng,et al., 2019]
	2.33 per 100,000 [Kalubowila et al., 2018]	0.09 per 100,000 [Niriella, et al., 2019]
Indonesia	—	0.27 per 100,000 [Ng,et al.,2019]
Philippines	—	0.14per 100,000 [Ng,et al.,2019]



## 3.2 Crohn's diagnostic and treatment capacity in LLMICs

OF THE 216 STUDIES included in the review, 112 discussed the utilization of diagnostic and treatment services, all of which include cases that were confirmed via both colonoscopy and histology (Table 4). Of the 21 LLMICs included, all but Bolivia and Syria had at least one study discussing the utilization of Crohn's diagnostic services: blood testing, stool testing, TB testing, radiology/imaging, endoscopy, and pathology services. South Asian countries reported the highest utilization of diagnostic services, with only Nepal lacking studies mentioning stool testing and TB testing (Table 4, Appendix 1.4 for numbers of studies reporting utilization of Crohn's disease diagnostic and treatment services from each country). Included LLMICs in the Middle East and North Africa all had multiple studies reporting the utilization of endoscopy, radiology, and stool testing, however only one study from Egypt mentioned TB testing (Appendix 1.4). Studies from sub-Saharan Africa also mentioned TB testing less frequently compared to those from South Asia, with only two of the 16 included sub-Saharan African countries having studies discussing it in this context (Table 4). Twelve studies (five from India<sup>6,10,43,44,45</sup>, two from Tunisia<sup>46,47</sup>, and one each from Egypt<sup>48</sup>, Nepal<sup>49</sup>, Sudan<sup>50</sup>, Ethiopia<sup>51</sup>, and Cameroon<sup>52</sup>) described Crohn's being diagnosed surgically or on autopsy (Table 4). Two studies, one a multi-country study from Asia and one from Nigeria, mentioned that only a clinical diagnosis of Crohn's disease was made without endoscopic and pathologic investigation unless multiple diseases were suspected. In India, a failed trial of anti-tubercular therapy (ATT) was mentioned in 11 studies as an important part of diagnosing Crohn's disease (Table 4). Two studies from Pakistan, and one study each from Ethiopia and Malawi, also discussed first treating their patients with ATT to aid in Crohn's disease diagnosis. It is important to note that many countries only have one

or two included studies, so the absence of diagnostics mentioned might reflect a lack of academic research rather than a true lack of diagnostic capacity in those countries (Appendix 1.4).

OF THE 21 LLMICS included, all but Bolivia, Ghana, and Syria had at least one study discussing the utilization of one or more Crohn's medications or surgical treatments (Table 5). Corticosteroids, aminosalicylates, and immunomodulators are the most frequently reported medications overall, while biologic agents are the least available (Appendix 1.4). Studies from India, Pakistan, Sri Lanka, Tunisia, and Egypt report the use of medications in all major Crohn's medication categories, while those from Bangladesh, Morocco, Kenya, Uganda, and Vietnam did not mention any Crohn's medications (Table 5). The use of biologics was only discussed in 26 of the 216 studies, and were not mentioned in any studies from sub-Saharan Africa or East Asia & Pacific (Appendix 1.4). Nutritional therapy was also scarcely mentioned, with only six studies discussing dietary changes as a treatment for IBD: four from India<sup>53,54,55,56</sup>, one from Egypt<sup>57</sup>, and one from Malawi<sup>58</sup> (Appendix 1.4).

THE MOST FREQUENTLY discussed Crohn's surgery overall is colectomy, followed closely by small bowel resection (Appendix 1.4). Ileoanal pouches were not specifically described in any of the included studies, but several studies described other or unspecified anal surgery for Crohn's disease. Studies from Ghana<sup>59</sup>, Malawi, and the Philippines did not mention any Crohn's surgeries, and those from Bangladesh<sup>60</sup>, Morocco, Sudan, and Kenya discussed surgery but did not specify which types (Appendix 1.4). Again, it is important to note that those countries with higher numbers of included studies also report the greatest use of diagnostics, medications, and surgeries.

**Table 4.** Utilization of Crohn's disease diagnostic and treatment services reported in studies included in the review by region and country

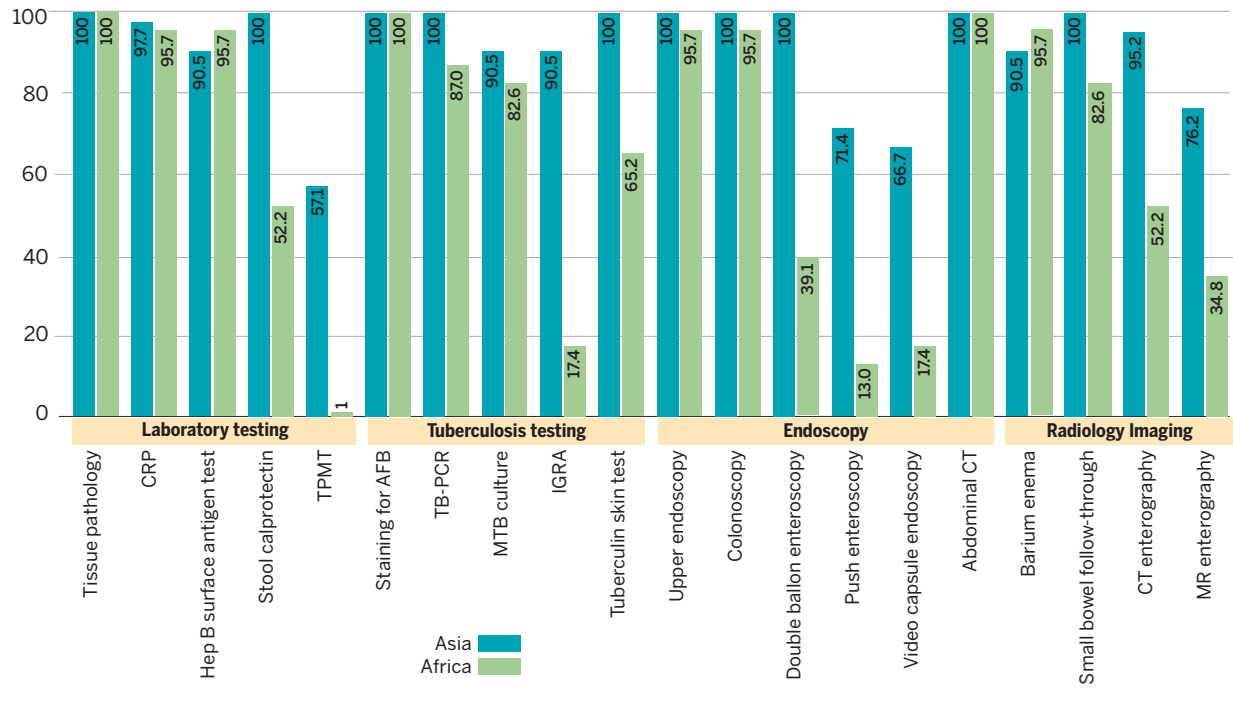
Region/Country	Diagnostics							Medical						Surgical					
	Endoscopy	Pathology	Radiology	Blood Testing	Stool Testing	Trial of ATT	Surgical/autopsy diagnosis	Clinical diagnosis only	TB Testing	Corticosteroids	Aminosalicyclates	Immunomodulators	Biologicagents	Nutritional therapy	Colectomy	Ostomy	Small bowel resec-	Ileoanal pouch	Strictureplasty
<b>Overall (N=216)</b>	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
<b>South Asia (N=129)</b>	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
India (N=107)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X
Sri Lanka (N=11)	X	X	X	X	X	X			X	X	X	X	X		X	X	X		X
Pakistan (N=9)	X	X	X	X	X			X	X	X	X	X	X		X	X			
Nepal (N=3)	X	X	X	X			X	X		X		X	X		X		X		
Bangladesh (N=2)		X	X					X	X										
<b>Middle East &amp; North Africa (N=67)</b>	X	X	X	X	X		X		X	X	X	X	X	X			X	X	X
Tunisia (N=41)	X	X	X	X	X		X		X	X	X	X	X		X		X	X	X
Egypt (N=18)	X	X	X	X	X		X		X	X	X	X	X		X	X			
Morocco (N=7)	X	X	X	X	X														
<b>sub-Saharan Africa (N=16)</b>	X	X	X	X	X	X	X	X	X	X	X	X			X		X	X	X
Nigeria (N=5)	X	X	X	X	X			X	X		X						X		
Sudan (N=3)	X	X	X	X	X		X		X	X	X								
Ethiopia (N=2)	X	X	X	X	X	X	X			X	X				X		X		
Kenya (N=2)	X	X																	
Uganda (N=1)		X		X	X		X										X		
Ghana (N=1)	X	X	X	X	X														
Cameroon (N=1)	X		X	X						X	X	X			X				
Malawi (N=1)	X	X	X	X	X	X				X		X		X					
<b>East Asia &amp; Pacific (N=5)</b>	X	X	X							X	X				X		X		
Indonesia (N=3)	X	X	X								X						X		
Philippines (N=2)	X									X	X								
Vietnam (N=1)	X	X													X				

\*Studies from Bolivia and Syria did not report on diagnostic or treatment services availability.

**Table 5.** Number of studies reporting utilization of Crohn's disease diagnostic and treatment services by region and country

Region/Country	Diagnostic							Medical							Surgical						
	Endoscopy	Pathology	Radiology	Blood Testing	Stool Testing	TB Testing	Trial of ATT disc used	Surgical/autopsy diagnosis	Clinical diagnosis	Corticosteroids	Aminosalicylates	Immunomodulators	Biologics	Nutritional therapy	Colectomy	Ostomy	Small bowel resection	Ileoanal pouch	Stricturoplasty	Unspecified surgery	Other
<b>Overall (N=216)</b>	<b>112</b>	<b>110</b>	<b>109</b>	<b>117</b>	<b>75</b>	<b>45</b>	<b>15</b>	<b>12</b>	<b>2</b>	<b>77</b>	<b>66</b>	<b>54</b>	<b>26</b>	<b>6</b>	<b>26</b>	<b>6</b>	<b>23</b>	<b>-</b>	<b>5</b>	<b>26</b>	<b>36</b>
<b>South Asia (N=129)</b>	<b>74</b>	<b>66</b>	<b>64</b>	<b>58</b>	<b>37</b>	<b>42</b>	<b>13</b>	<b>6</b>	<b>1</b>	<b>49</b>	<b>40</b>	<b>41</b>	<b>22</b>	<b>4</b>	<b>17</b>	<b>5</b>	<b>13</b>	<b>-</b>	<b>4</b>	<b>15</b>	<b>26</b>
India (N=107)	57	50	50	51	32	37	11	5	-	39	36	36	17	4	12	3	11	-	3	13	20
Sri Lanka (N=11)	7	4	4	3	2	2	-	-	-	5	2	3	3	-	2	1	-	-	-	1	1
Pakistan (N=9)	8	7	5	3	2	1	2	-	-	4	2	2	1	-	2	1	1	-	1	-	2
Nepal (N=3)	2	3	3	1	-	-	-	1	-	1	-	1	1	-	1	-	1	-	-	-	2
Bangladesh (N=2)	-	2	2	-	1	2	-	-	1	-	36	36	-	4	-	3	-	-	-	1	1
<b>Middle East &amp; North Africa (N=67)</b>	<b>22</b>	<b>29</b>	<b>31</b>	<b>48</b>	<b>12</b>	<b>1</b>	<b>-</b>	<b>3</b>	<b>-</b>	<b>20</b>	<b>18</b>	<b>11</b>	<b>4</b>	<b>1</b>	<b>7</b>	<b>-</b>	<b>6</b>	<b>-</b>	<b>1</b>	<b>11</b>	<b>4</b>
Tunisia (N=41)	24	15	17	30	2	-	-	2	-	15	13	8	3	-	5	-	5	-	1	10	1
Egypt (N=18)	15	12	12	14	9	1	-	1	-	5	5	3	1	1	2	-	1	-	-	-	2
Morocco (N=7)	5	2	3	4	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	1
<b>sub-Saharan Africa (N=16)</b>	<b>11</b>	<b>12</b>	<b>10</b>	<b>11</b>	<b>9</b>	<b>2</b>	<b>2</b>	<b>3</b>	<b>1</b>	<b>7</b>	<b>6</b>	<b>2</b>	<b>-</b>	<b>1</b>	<b>1</b>	<b>1</b>	<b>3</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>7</b>
Nigeria (N=5)	3	4	3	4	4	-	-	-	1	4	3	-	-	-	-	-	1	-	-	-	2
Sudan (N=3)	2	2	2	1	1	1	-	1	-	1	1	-	-	-	-	-	-	-	-	-	1
Ethiopia (N=2)	2	2	2	2	1	-	1	1	-	1	1	-	-	-	1	-	1	-	-	-	2
Kenya (N=2)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1
Uganda (N=1)	-	1	-	1	1	-	-	1	-	-	-	-	-	-	-	-	1	-	-	-	-
Ghana (N=1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Cameroon (N=1)	1	-	1	1	-	1	-	-	-	-	1	1	-	-	-	1	-	-	-	-	1
Malawi (N=1)	1	1	1	1	1	-	1	-	-	1	-	1	-	1	-	-	-	-	-	-	-
<b>East Asia &amp; Pacific (N=5)</b>	<b>5</b>	<b>3</b>	<b>3</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>1</b>	<b>2</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>1</b>	<b>-</b>	<b>1</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>1</b>
Indonesia (N=3)	3	2	3	-	-	-	-	-	-	-	1	-	-	-	-	-	1	-	-	-	1
Philippines (N=2)	1	-	-	-	-	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-
Vietnam (N=1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	1	-	-	-	-	-	-

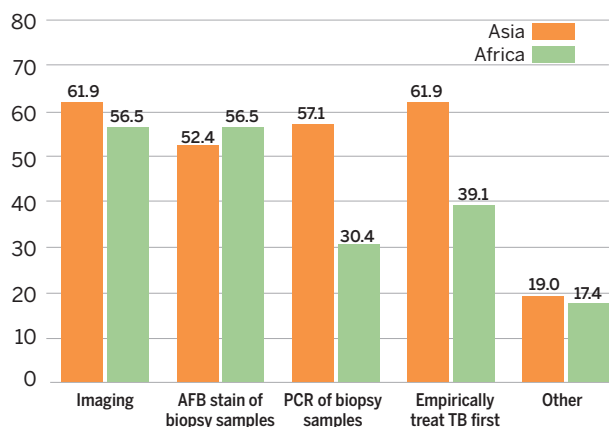
**Figure 7.** Availability of Crohn's diagnostic technology in LLMICs, overall and by region



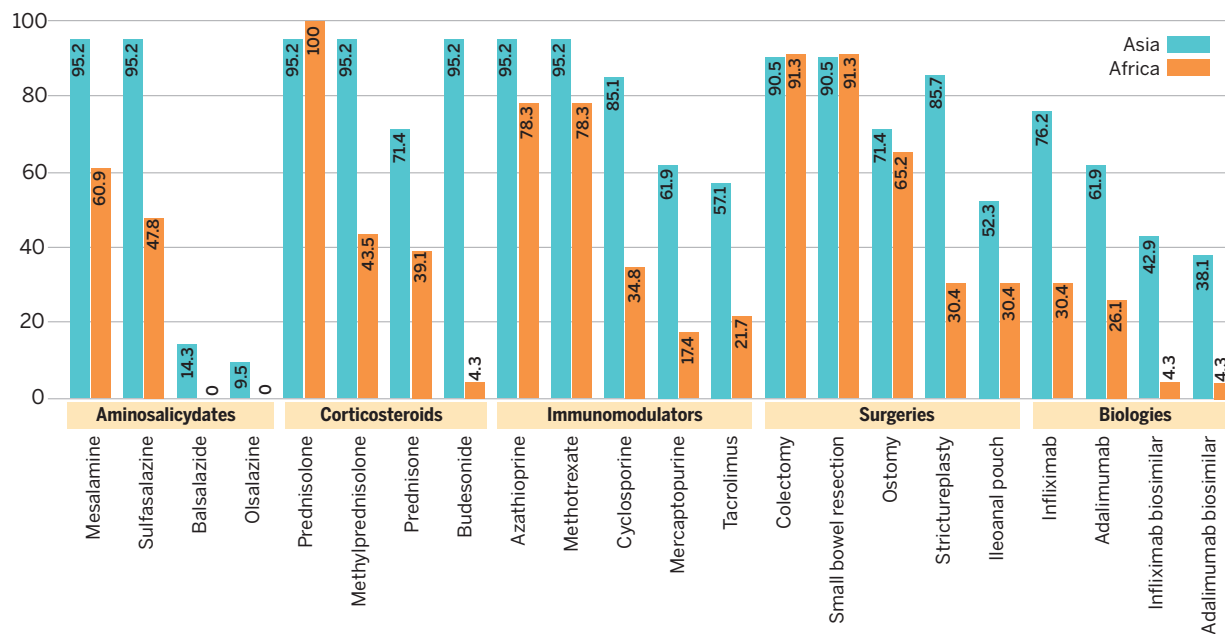
ALL OR MOST of the providers who participated in the provider survey reported having access to basic Crohn's diagnostic testing such as tissue pathology, Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), TB testing modalities, upper endoscopy, colonoscopy, X-ray, barium enema, small-bowel follow-through, and abdominal CT scans (**Figure 7, Appendix 2.3**). Of note, stool calprotectin was widely available to respondents from Asian LLMICs but only half of providers from Africa. Similarly, endoscopic ultrasound was reported to be available to all providers who responded from Asia, compared with only 36.4% of African participants. Video capsule endoscopy is the least available advanced endoscopic procedure, especially in Africa, with only 40.9% of respondents having access overall (66.7% in Asia, 17.4% in Africa). Advanced imaging technology such as CT enterography is available to most respondents from Asia and half from Africa, and MR enterography is available to 76.2% of respondents from Asia and 34.8% from Africa. Respondents from Malawi, Rwanda, Kenya, and Zimbabwe all did not have access to CT or MR enterography, though sample sizes are small (**Appendix 2.3**).

DIFFERENTIATION BETWEEN Crohn's disease and intestinal Tuberculosis (ITB) is a major challenge in LLMICs due to the high prevalence of TB in Africa and South Asia. For both Asian and African providers, the most frequently used methods for distinguishing between Crohn's disease and ITB are imaging (59.1% of providers overall) and AFB stain of biopsy samples (54.5% of providers overall) (**Appendix 2.5**). Asian providers reported using considerably more empirical treatment of TB before

**Figure 8.** How providers in LLMICs differentiate between Crohn's disease and intestinal tuberculosis



**Figure 9.** Availability of Crohn’s treatments in LLMICs, overall and by region



considering Crohn’s (61.9% vs. 39.1%) as well as PCR of biopsy samples (57.1% vs. 30.4%), compared to African providers.

FIRST LINE CROHN’S MEDICATIONS, such as Prednisolone, Mesalamine, Sulfasalazine, and Azathioprine, are widely reported to be available by providers across all the included LLMICs (**Appendix 2.6, Figure 9**). The two most critical Crohn’s surgeries, colectomy and small bowel resection, are also commonly available to the providers surveyed. The availability of more advanced surgeries and alternative medications are much more variable across world regions and from country to country. Biologic agents Infliximab and Adalimumab were reportedly available to most providers in Asia (76.2%), compared to 31.8% of respondents from Africa. Participants from Ethiopia, Malawi, or Rwanda did not report availability of any biologic agents (**Appendix 2.6**).

MOST OF THE HOSPITALS we visited in both Asia and Africa had all or many of the facilities necessary for diagnosing Crohn’s disease. Every hospital we visited in Asia had endoscopy and colonoscopy

facilities, and only Raipur Medical College lacked ERCP and endoscopic ultrasound technology because they did not have any gastroenterologists on staff and all endoscopy and colonoscopy was done by surgeons. All the facilities had access to necessary radiology such as small bowel follow-through, abdominal CT, and CT enterography. MR enterography was available in eight of the 14 Asian hospitals we visited, but it was rarely used by most of the providers we spoke to due to its high cost. CT enterography was preferred by providers but was also cost prohibitive to some patients. Stool calprotectin was available at most of the hospitals in India and Pakistan but was also rarely done due to very high cost, and in Nepal is only available at outside private pathology facilities. TB-PCR was also available at all facilities but was not widely used or trusted due to high rates of false positives as a result of contamination.

IN AFRICA, all the tertiary hospitals we went to had endoscopy and colonoscopy facilities, but endoscopy was not available at Neno District Hospital in Malawi. Only one of the six hospitals performed advanced endoscopic procedures such as ERCP or endoscopic ultrasound (EUS), Black Lion Hospital

in Addis Ababa. Another diagnostic challenge noted in all three countries was lack of access to fecal calprotectin testing. Radiology was also more limited in the African countries we visited compared to the Asian countries we visited, and while all had access to abdominal CT and X-ray, none of the hospitals had MR or CT enterography in their facility. TB testing modalities were generally considered to be futile due to the very high prevalence of TB in these settings.

MOST FACILITIES WE VISITED in Asia had access to basic Crohn's medications such as aminosalicyclates (mesalamine and sulfasalazine), steroids (budesonide and prednisone), and immunomodulators (azathioprine and methotrexate). Most facilities in India had access to biologics such as Infliximab and Adalimumab and their biosimilars, but these medications are cost prohibitive to the vast majority of patients

and also increase the risk of TB reactivation, so they are not widely used. Brand name Infliximab and Adalimumab were reported to be available to providers in Pakistan, but not their less expensive biosimilars. Biologics are not approved in Nepal and thus can only be imported from India, making them even more expensive and thus inaccessible to patients. Most of the gastroenterologists we met in Nepal had either never used biologics or had only used them in a handful of patients.

IN AFRICA, most facilities had access to basic steroids such as Prednisone and immunomodulators such as Methotrexate but were very limited in all other drug categories. None of the hospitals had access to Sulfasalazine, Budesonide, or any form of biologics (Infliximab, Adalimumab). Half of the facilities had access to Azathioprine, and only one (CHUK) had Mesalamine.

### 3.3 Socioeconomic characteristics of individuals with Crohn's disease in LLMICs

OF THE 216 STUDIES in 21 countries included in this review, only 29 studies in 11 countries discussed patient geographic, socioeconomic, or cost information (see **Appendix 1.5** for a summary of patient geographic residency, socioeconomic characteristics, insurance coverage, and out of pocket costs). India had the most information due to the large number of available publications. All eight<sup>5,7,9,10,11,15</sup> of the studies from India that discussed patients' geography reported that more individuals with Crohn's resided in urban areas compared to rural areas (see **Appendix 1.5**). Similarly, studies from Egypt<sup>13</sup>, Ethiopia<sup>14</sup>, and Indonesia<sup>15</sup> report individuals with Crohn's coming from cities more frequently. Sri Lanka, on the other hand, has a recent study reporting more cases among rural communities (73.9%) than urban (26.1%).<sup>16</sup> Two older studies from Bolivia in 1975<sup>17</sup> and Kenya in 1980<sup>18</sup> also describe

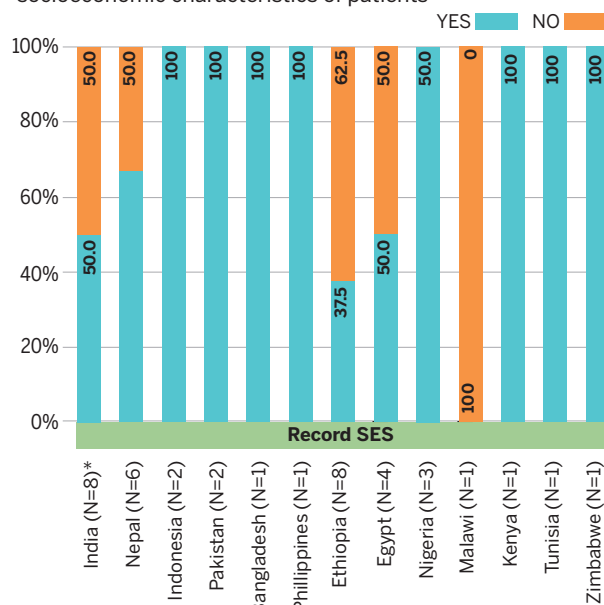
more rural Crohn's patients than urban. Only eight studies from three of the included countries reported on socioeconomic characteristics, either income level, education level, or employment status: India, Tunisia, and Sudan (**Appendix 1.5**). Four of the five Indian studies, as well as the one from Sudan<sup>19</sup>, reported that most individuals with Crohn's disease belong to the middle or upper class and have relatively high level of education. In contrast, one study from India reported that the majority of individuals with Crohn's are non-graduates (62.6%), are unemployed or unskilled workers (62.3%), and have an annual family income of less than 1000000 INR (~\$14K USD) (83.8%).<sup>7</sup> One Tunisian study from 2014 discussing socioeconomic characteristics reported that over half of the patients had a university education,<sup>21</sup> whereas another in 2017 reported that 22.2% had a university education.<sup>46</sup>

This study also reported that 34.3% of patients had “bad” socioeconomic conditions, 49% had “good” socioeconomic conditions, and 16.7% had “well” socioeconomic conditions.<sup>46</sup>

THREE STUDIES from India and two from Nigeria describe out of pocket costs and insurance coverage of individuals with Crohn’s Disease (**Appendix 1.5**). Both of the studies from Nigeria reported that national health insurance programs are available but that coverage is limited, so all treatments were paid for out of pocket by patients.<sup>62,63</sup> Studies from India were more variable, with one from 2009 explaining that cost of medications was not a factor,<sup>55</sup> another in 2017 reporting that 60% of patients were covered by private insurance,<sup>43</sup> and most recently in 2019 where 14.3% of patients discontinued Adalimumab due to high cost.<sup>20</sup>

OF THE 39 SURVEY participants who responded to the question regarding whether they record some form of information about socioeconomic characteristics of patients, which may include class, income level, or occupation, 64.1% of which reported that they do (**Figure 10**). All the providers from Indonesia, Pakistan, Bangladesh, the Philippines, Nigeria, Kenya, Tunisia, and Zimbabwe reported that they did record socioeconomic information, whereas

**Figure 10.** Proportion of providers who do and do not record socioeconomic characteristics of patients



\*Missing data from 6 responses excluded: 2 from India, 1 from Malawi, 2 from Rwanda, 1 from Sudan

providers from Ethiopia and Malawi report the lowest frequencies of recording socioeconomic data (**Figure 10**).

MOST OF THE SURVEY participants overall estimated that approximately 26-50% of their patients diagnosed with Crohn’s live in rural areas. When stratified by region, Asian providers reported somewhat higher proportions of their patients living in rural areas. ■



## 3.4 Challenges and barriers to providers and individuals with Crohn's disease in LLMICs

**Table 6.** Most frequently reported diagnostic, management, access, and financial challenges and barriers to Crohn's patients and providers in LLMICs

Diagnostic Challenges	# of countries	# of studies
Difficulty differentiating between CD and ITB	10	42
Difficulty differentiating between CD and thier infectious diseases	9	32
Low disease index of suspicion/clinical awareness due to preceived rarity of IBD leads to underdiagnosis	11	26
Lack of quality diagnostic facilities and investigational modalities	8	12
Difficulty differentiating between CD and UC	4	6
Diagnosis of CD made on histological exam of resected colon	3	4
Lack of reliable TB testing modalities	3	3
Management Challenges		
Use of biologics is limited due to cost	2	11
High risk of TB infection reactivation in patients treated with biologic	1	1
Access Barriers		
Lack of access to high quality health care services	4	9
Lack of access to IBD medications	2	5
Lack of education/knowledge about disease	3	3
Lack of access to psychosocial support	2	3
Low sanitation level	2	2
Financial Barriers		
Patients unable to afford treatment in general (medications and surgeries)	7	20
Patients unable to afford biologics	2	11
High cost of diagnostic testing	4	5
Lack of insurance coverage	2	4

Cost of Crohn's care

OF THE 21 LLMICs included in this review, 14 hypothesized at least one specific diagnostic, management, access, or financial challenge or barrier to individuals with Crohn's disease and providers (see **Appendix 1.6** for a summary of diagnostic, management, access, and financial challenges and barriers to individuals with Crohn's

and providers in LLMICs). The most commonly reported provider challenge is differentiating between Crohn's and intestinal tuberculosis (ITB), due to the high prevalence of TB in LLMICs and its overlap of symptoms and endoscopic features. This can result in long delays in disease diagnosis and thus appropriate treatment. A total of 36 studies in



**Table 7.** Ranges of costs to patients of common Crohn's disease treatments

Hospital for Crohn's flare							
	<\$100	\$101-500	\$501-1000	\$1001-2000	\$2001-5000	>\$5000	Missing
<b>Overall (N=43)*</b>	<b>5 (11.6)</b>	<b>17(39.5)</b>	<b>4 (9.3)</b>	<b>5 (11.6)</b>	<b>1 (2.3)</b>	<b>1 (2.3)</b>	<b>10 (23.3)</b>
Asia total (N=21)*	1 (4.8)	8(38.1)	2 (9.5)	1 (4.8)	-	1 (4.8)	8 (38.1)
Africa total (N=22)*	4 (18.2)	9 (40.1)	2 (9.1)	4(18.2)	1(4.5)	-	2 (9.1)
Biologic Agents							
	<\$50	\$50-100	\$100-500	>\$500	Missing		
<b>Overall (N=43)*</b>	<b>2 (4.7)</b>	<b>4(9.3)</b>	<b>12 (27.9)</b>	<b>14 (32.6)</b>	<b>11 (25.6)</b>		
Asia total (N=21)*	1 (4.8)	8(38.1)	4 (19.0)	8 (38.1)	6 (28.6)		
Africa total (N=22)*	4 (18.2)	9 (40.1)	8(36.4)	6 (27.3)	5 (22.7)		

\*Two missing responses from Sudan and one missing response from India excluded  
All values presented as mean (percent)

10 countries in the review included distinguishing between Crohn's and ITB as a diagnostic challenge to providers (**Table 6**). This was followed by diagnostic delays due to perceived rarity of Crohn's and lack of clinical awareness among providers, which was mentioned in 17 studies from eight countries, and lack of quality diagnostic facilities, which was mentioned in 14 studies from eight countries. Management challenges to Crohn's providers were discussed less frequently than diagnostic challenges, with three studies reporting limited use of biologics due to cost, and one reporting risk of TB reactivation on biologics.

THE MOST frequently reported patient barrier was cost of Crohn's surgeries and medications, particularly biologics. Patients' inability to afford the costs of their treatment in general was mentioned in nine studies, and high cost of biologics specifically in three studies (**Table 6**). Lack of access to high quality health care facilities was another common patient barrier, with nine studies describing access to care as a patient barrier.

## Costs of Crohn's care

COLONOSCOPY WITH BIOPSY and upper endoscopy

with biopsy in both Asia and Africa were reported by the most providers for a cost range less than US \$50 (**Appendix 2.8**). Abdominal CT scans are more costly to patients, with most falling in the US \$50-100 range, and one provider in Malawi reporting it costing more than US \$500 (**Appendix 2.8**). Basic stool testing is considerably less expensive, with most providers reporting costs to patients under US \$25. It should be noted there is a substantial amount of missing data for the cost-related survey questions. In addition, these costs should be seen in the light of total health expenditure per capita of \$44 in low-income countries and \$80 in lower-middle income countries.

OVERALL, THE MOST frequently reported cost of a hospitalization for a Crohn's disease flare was between US \$101 and \$500 (39.5%) (**Table 7**). One provider in Pakistan reported that being hospitalized for a Crohn's flare could cost a patient over US \$5,000 (**Appendix 2.9**). The most frequently reported cost of biologics overall is over US \$500 (32.6%), followed closely by the US \$100-500 category (27.9%) (**Table 7**). It should again be noted there is a substantial amount of missing data for the cost-related survey question.

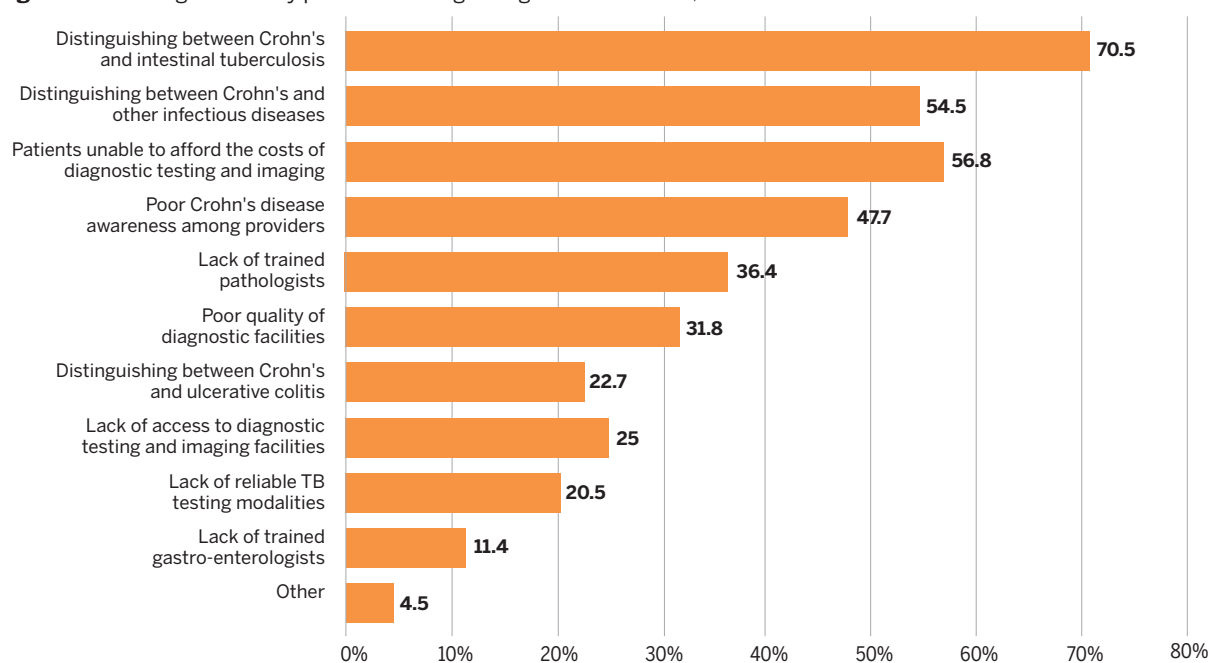
## Challenges to Providers

THE MOST COMMONLY reported challenge in diagnosing Crohn’s disease overall is differentiating between Crohn’s and ITB, particularly in Asian countries where it was reported by 90% of providers (Figure 11). Distinguishing between Crohn’s and other infectious diseases was also frequently reported in both Asia and Africa, as well as patients’ inability to afford the cost of diagnostic testing (Figure 12). Gastroenterologists in Africa particularly struggle with poor Crohn’s disease awareness among providers

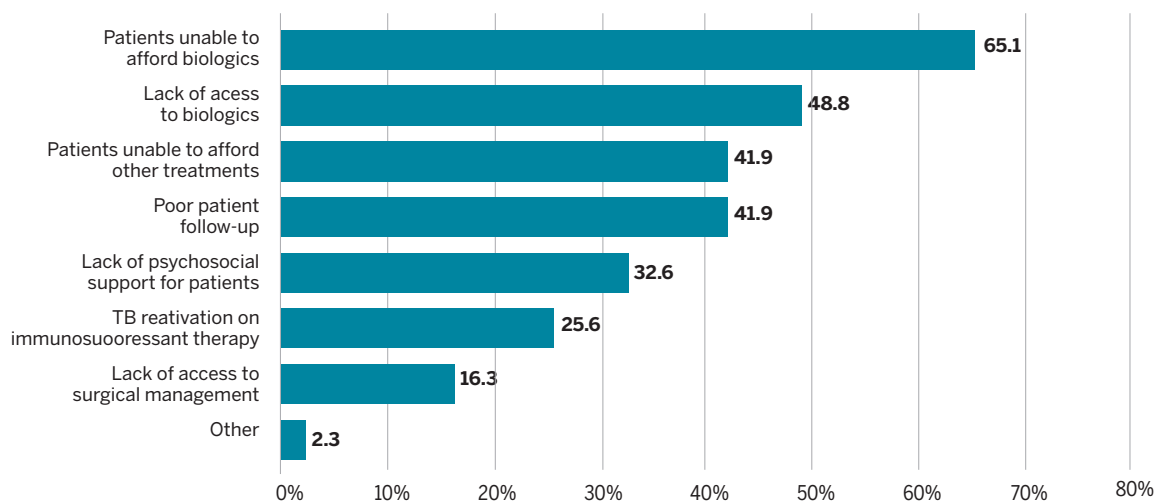
(66.7%) and lack of trained pathologists (61.1%) in accurately diagnosing Crohn’s.

THE MOST COMMONLY reported challenge in managing Crohn’s disease overall is patients’ inability to afford biologics, particularly in African countries where it was reported by 72.7% of providers (Figure 13). Unlike Asia, lack of access to biologics is also a highly reported challenge for African gastroenterologists (68.2%), as is poor patient follow-up (54.5%).

**Figure 11.** Challenges faced by providers in diagnosing Crohn’s disease, across all LLMICs



**Figure 12.** Challenges faced by providers in managing Crohn’s disease, across all LLMICs



# patient profiles

At many of the institutions that we visited, we had a chance to talk to Crohn's disease patients who were currently hospitalized.



## 4.1 India

While visiting AIG's IBD clinic, we had the chance to talk to a young Crohn's patient and her mother. The patient was a 14-year-old girl, named M here to protect her privacy, who was diagnosed with Crohn's in March 2017 at the age of 12.

When M was diagnosed, she was malnourished due to vomiting, diarrhea, and an inability to eat, and was suffering from abdominal pain and rectal bleeding. She is currently taking Azathioprine with some improvement but continues to be symptomatic. Having Crohn's has severely impacted M's quality of life, in that she looks like a young child despite being 14, has not yet had her menstrual period, and is unable to eat. M and her mother were very poor and live a one-hour bus ride outside of Hyderabad. Cost of Crohn's diagnostics and treatment was a major barrier to M, and "what will we have to pay?" was a constant question by her mother. Dr. Banerjee expressed that M is a patient who could likely significantly benefit from biologic therapy, but she cannot receive it due to her family's inability to afford the treatment.

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We also met several Crohn's disease patients in the in-patient ward at AIIMS. The first patient was a 45-year-old woman who was there with her teenaged daughter. She was originally diagnosed with UC in 2001, when she started having loose bowel movements 8-9 times per day after her pregnancy. Her diagnosis was changed to Crohn's in 2009 when she had a bowel perforation and had to undergo emergency surgery. She has been managing her illness with mesalamine and prednisone for the last eight years but continues to have loose bowel movements and weight loss. The patient reported she will be starting Infliximab soon, and that the government will cover 75% of the cost because she is poor. The most challenging aspect of her disease she faces is the need for regular follow-up every 2 months. She lives in a medium-sized town that is 3-4 hours away from Delhi by train, and there is no GI specialist in her area. Because her husband passed away last year, her daughter must leave school to accompany her to her appointments at AIIMS.

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We then met a 51-year-old man from Delhi who had been hospitalized at AIIMS for almost a month with an anal fistula. He was symptomatic with chronic diarrhea since 2002, but was not diagnosed with Crohn's until 2015 by abdominal CT. He explained that his symptoms were dismissed by numerous doctors over the years and he was repeatedly treated with different antibiotics without the recommendation for a colonoscopy or any other testing.

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The last patient we met at AIIMS was another 45-year-old woman, also from Delhi, recently diagnosed with Crohn's. She explained that she was currently doing well on biologics, but endured years of severe symptoms and misdiagnosis before coming to AIIMS. Her symptoms of loose bloody stools started in 2005, at which time she was treated for hemorrhoids with both drugs and surgery at a private clinic. Since that time, she has been seen at numerous hospitals and clinics, and was diagnosed with Crohn's only recently when she was referred to AIIMS for surgical consultation for a distended abdomen. She has since had two doses of biologics and follows-up every three months, and her bleeding has completely resolved.

## 4.2 Nepal

At Nidan Hospital, we had the chance to speak with one of Dr. Neeraj Joshi's long-time Crohn's disease patients, a 50-year-old man named S. He was diagnosed with Crohn's 20 years ago due to a bowel obstruction, 4-5 years after having surgery for a burst appendix. He manages his disease with dietary modifications, vitamins, and prednisone as needed for flares. He explained that when he has a flare, he gets severely constipated and must be on a liquid diet for a 2-3 weeks and take prednisone to manage his symptoms. S noted he feels very dependent on steroids and is reluctant to be on them long-term, and wonders if he can be weaned off the steroid and start an alternative treatment. S described himself as middle-class and expressed that Nidan Hospital is easily accessible from his home in Nepal. However, he pays entirely out of pocket for his Crohn's disease care, which is usually 5-10,000 Nepalese rupees (\$50-100 USD) per month. S also expressed that he does not know anyone else with Crohn's disease, and thinks he would benefit from the establishment of a Crohn's or IBD club in Nepal where patients with similar conditions can share their experiences and support each other.

## 4.3 Ethiopia

Although Crohn's patients are few and far-between in Malawi and Rwanda, we were able to speak to two IBD patients in Ethiopia. The first was an inpatient at Black Lion Hospital with severe UC – a 55-year-old man from Addis. He had been hospitalized for repeated lower gastrointestinal symptoms that had worsened in recent months. His diagnosis was delayed, and he was treated with antibiotics, repeatedly admitted to the ICU, and had multiple blood transfusions before finally receiving a diagnosis at Black Lion after he was referred due to the severity of his symptoms. He is now on steroids with good response.

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The most impactful patient we have met was a medical intern at Saint Paul's Hospital, who was also recently diagnosed with Crohn's disease while she was in medical school. The diagnosis took eight months to confirm, and during a very severe flare she considered quitting school as her professors didn't understand her need for time off. It was at that time that she joined a U.S.-based Crohn's support group on Facebook, giving her the chance to communicate with other Crohn's patients about what she was experiencing. This helped motivate her to continue medical school, and also inspired her to create a similar platform in the local language. Lack of awareness and social stigma are major barriers to Crohn's patients in Ethiopia due to the symptoms and autoimmune processes that are difficult to explain to non-medical family and friends. To help patients like her, the new doctor is currently establishing a Crohn's support group in Addis online and on messaging apps such as WhatsApp and Telegram. She is hoping to eventually expand outside of Addis, and also noted that most Crohn's patients in Ethiopia probably don't have access to a computer or smartphone and is looking into alternative mediums for the group to reach those patients. In addition to the social aspects of managing Crohn's disease, she also talked about the high cost of Crohn's medications as a major barrier to patients in Ethiopia. After her diagnosis, she was on Prednisone for 3 months, and then switched to Azathioprine for maintenance. She explained that Azathioprine must be imported, and a single 50mg pill costs her 20 birr (approximately \$0.68 US), which adds up very quickly and is a substantial burden for most Ethiopian Crohn's patients.

In addition, she was able to offer a unique perspective as both a provider and patient. In her clinical experience, she has cared for 30-50 patients with IBD, most of which were diagnosed with Crohn's. She explained that most of the patients she's seen arrive with end-stage

complicated disease, presenting with perforations and fistulas that often require surgery or palliative care. Her impression is that IBD patients with milder symptoms are more likely to prefer traditional or herbal medications before coming to the hospital. She also explained that this is exacerbated by misdiagnosis, giving an example of a patient from 70 km outside of Addis who was seen at a peripheral hospital for severe abdominal pain, weight loss, and diarrhea, referred to a hospital in Addis with suspected Crohn's, and was given antibiotics and sent home. He later returned to Addis with an enterocutaneous fistula due to Crohn's disease. Speaking with this young woman was perhaps the most meaningful experience of our site visits, and we were so inspired by her passion and drive to help others as both a new physician and a Crohn's disease patient herself.



There appears to be more Crohn's disease in LLMICs than is indicated in the literature. It is critical to study and publish data on Crohn's disease in LLMICs, even if they are facility-based or case studies, and to set up clinical data registries so that population-based epidemiologic research can shed light on the true burden of Crohn's disease in these settings.

## **conclusion**





The mean number of patients diagnosed with Crohn's cared for in the last year was 89.5 overall and varied widely from 0 reported at one facility in Rwanda, to 1,000 reported at two different facilities in India.

Crohn's disease made up 21% of the inflammatory bowel disease diagnoses reported with Africa having a larger proportion of Crohn's compared to ulcerative colitis than Asia.

Most of the providers reported that patients with Crohn's have symptoms for between 6 and 24 months prior to diagnosis and that 26-50% of their patients live in rural areas.

The most common challenges to managing Crohn's disease in LLMICs are differentiating between Crohn's and tuberculosis, poor disease awareness, lack of trained pathologists and patients' inability to afford biologics.

## 5.1 summary of findings

### Burden of Crohn's Disease in LLMICs

MOST (73.4%) of the LLMICs do not have any studies describing individuals with Crohn's disease (**Figure 4**), highlighting a major lack of published data. There is an even more severe lack of population-based epidemiologic data with only four LLMICs reporting any incidence or prevalence data—India, Indonesia, Sri Lanka, and the Philippines—all of which are in Asia.

OVERALL, the mean number of cases of Crohn's disease reported per study is 57.84 but varies widely from single-patient case studies in some countries to cohorts of as many as 980 individuals in India (**Table 1**).

OUR CROSS-SECTIONAL SURVEY of gastroenterology providers in countries where the poorest billion live had a total of 46 (54.8%) participants from 15 countries, representing 33, mostly public and urban, health facilities with three (9.4%) being located in rural areas.

OVERALL, the mean number of patients diagnosed with Crohn's, cared for in the last year by survey respondents, was 89.5 and varied widely from 0 reported at one facility in Rwanda, to 1,000 reported at two different facilities in India (**Table 2**).

OVERALL, Crohn's disease made up 20.6% of the IBD diagnoses reported by survey respondents. This percentage also varied between countries and regions, with Africa having a larger proportion of Crohn's (43.4%) compared to UC than Asia (19.2%).

THERE APPEARS to be more Crohn's disease in LLMICs than is indicated in the literature<sup>44</sup>. This is particularly true for Ethiopia, which has virtually no

published IBD data but is seeing increasing patients being diagnosed with IBD and one of the highest proportions of Crohn's (69.4%) compared to UC of the included countries.

THIS GAP IN RESEARCH and reporting might be reflective of providers' lack of resources and incentives for publishing data, rather than a true absence of Crohn's disease in these populations. In addition, health management information systems in these countries may not be reliable or may not require routine reporting or surveillance of Crohn's disease.

IT IS CRITICAL to study and publish data on Crohn's disease in LLMICs, even if they are facility-based or case studies, and to set up clinical data registries so that population-based epidemiologic research can shed light on the true burden of Crohn's disease in these settings.

### Crohn's Diagnostic and Treatment Capacity in LLMICs

OF THE 21 LLMICS included in our scoping review, all but Bolivia and Syria had at least one study discussing the utilization of Crohn's diagnostic services: blood testing, stool testing, TB testing, radiology/imaging, endoscopy, and pathology services. All but Bolivia, Ghana, and Syria had at least one study discussing the utilization of one or more Crohn's medications or surgical treatments (**Table 4**).

CORTICOSTEROIDS, aminosalicylates, and immunomodulators are the most frequently reported medications overall, while biologic agents are the least available (**Appendix 1.4**). It should be noted that all of the studies in our scoping review, except one from a community hospital in Bolivia, were from large tertiary referral or specialty hospitals, associated with a university or the military. Thus, the availability

of these diagnostic tests at these tertiary referral facilities may not necessarily reflect the general standard of care across these countries; they likely reflect the research environment at these institutions.

MOST OF THE PROVIDERS reported that patients with Crohn's have symptoms for between 6 and 24 months prior to diagnosis.

FIRST LINE CROHN'S MEDICATIONS, such as Prednisolone, Mesalamine, Sulfasalazine, and Azathioprine, are widely reported to be available by providers across all of the included LLMICs (Figure 9). The two most critical IBD surgeries, colectomy, and small bowel resection, are also commonly available to the providers surveyed. The availability of more advanced surgeries and alternative medications are much more variable across world regions and from country to country. Biologic agents Infliximab and Adalimumab were reportedly available to most providers in Asia (76.2%), compared to 31.8% of respondents from Africa.

## Socioeconomic Characteristics of Individuals with Crohn's and Costs of Crohn's Care in LLMICs

OF THE 216 studies in 21 countries included in this review, only 29 studies in 11 countries discussed patient geographic, socioeconomic, or cost information (Appendix 1.5)

MOST OF THE STUDIES from India that discussed geography reported that more IBD patients lived in urban cities compared to rural villages, while the rest reported approximately equal numbers of urban and rural patients<sup>64</sup>.

SRI LANKA is the only country where a recent study reported more IBD patients from rural areas than urban areas, with only 26% of their IBD patients residing in urban communities.

MOST OF THE SURVEY participants overall estimated that approximately 26-50% of their patients diagnosed with Crohn's live in rural areas (Figure 11). When stratified by region, Asian providers reported somewhat higher proportions of their patients living in rural areas.

COLONOSCOPY with biopsy and upper endoscopy with biopsy in both Asia and Africa were reported by the most providers for a cost range less than US \$50 (Appendix 2.8). Abdominal CT scans are more costly to patients, with most falling in the US \$50-100 range, and one provider in Malawi reporting it costing more than US \$500 (Appendix 2.8). Overall, the most frequently reported cost of a hospitalization for a Crohn's disease flare was between US \$101 and \$500 (39.5%) (Table 7). One provider in Pakistan reported that being hospitalized for a Crohn's flare could cost a patient over US \$5,000 (Appendix 2.9). The most frequently reported cost of biologics overall is over US \$500 (32.6%), followed closely by the US \$100-500 category (27.9%) (Table 4). It should be noted there is a substantial amount of missing data for the cost-related survey questions. In addition, these costs should be seen in the light of total health expenditure per capita of \$44 in low-income countries and \$80 in lower-middle income countries.

## Challenges & Barriers to Providers and Individuals with Crohn's in LLMICs

IN OUR SCOPING REVIEW as well as provider survey, the most commonly reported provider challenge is differentiating between Crohn's and intestinal tuberculosis (ITB), due to the high prevalence of TB in LLMICs and its overlap of symptoms and endoscopic features (Figure 8). This can result in long delays in disease diagnosis and thus appropriate treatment.

THIS WAS FOLLOWED by diagnostic delays due to perceived rarity of IBD and lack of clinical awareness among providers, which was mentioned in 17 studies from eight countries, and lack of quality diagnostic facilities, which was mentioned in 14 studies from eight countries.

THE MOST FREQUENTLY reported patient barrier was cost of Crohn's surgeries and medications, particularly biologics. Patients' inability to afford the costs of their treatment in general was mentioned in nine studies, and high cost of biologics specifically in three studies (**Appendix 1.6, Appendix 2.7**).

GASTROENTEROLOGISTS in Africa particularly struggle with poor Crohn's disease awareness among providers (66.7%) and lack of trained pathologists (61.1%) in accurately diagnosing Crohn's.

## 5.2 key recommendations

BASED ON A MULTI-PRONGED methodology including a scoping review of 216 studies from LLMICs, survey responses from 46 gastroenterology providers from 15 LLMICs, and site visits to 20 hospitals with endoscopy facilities in 6 countries, we offer the following recommendations for improving access to and quality of Crohn's disease care in LLMICs:

### **Decentralize diagnosis to lower-level facilities**

THERE IS A HUGE GAP in terms of diagnostic capacity at lower-level facilities (like district hospitals) that could be a potential opportunity for us to improve access to and quality of care of Crohn's disease in the Poorest Billion. In our conversations with providers in the public sector in India and Nepal, it was quite clear that lower-level facilities (e.g., district hospitals in rural areas) did not have endoscopic capacity. For example, it was quite telling that Raipur Medical

College, the main public medical school and hospital in Raipur, the capital of Chhattisgarh state in India (with a population of 25 million), did not have a single gastroenterologist. Providers at Bir Hospital, one of the main public tertiary facilities in Kathmandu, lamented that it was very difficult for poor rural patients who traveled from remote areas of the country, to wait two weeks after a consultation to have a colonoscopy carried out, because such diagnostic capacity was not available at district hospitals. In both Malawi and Rwanda, endoscopy was only available at a single, public, tertiary, referral hospital in the capital city. These were also the countries seeing the least number of Crohn's patients. In contrast, Ethiopia had significantly greater numbers of gastroenterologist and endoscopy centers with higher numbers of Crohn's patients. It is highly likely that under-diagnosis and lack of access to diagnosis plays a huge part in the low numbers of Crohn's patients in Malawi and Rwanda. There is a great need and opportunity to consider decentralization of endoscopy to lower-level facilities like provincial or district hospitals in these countries in order to increase access to Crohn's diagnostics. In this context, we could study various models of care including the provision of diagnostic endoscopy by surgeons or possibly provision of endoscopy via mobile vans.

NAGESHWAR REDDY, the founder of AIG, has started a Rural Healthcare Project that includes medical camps with mobile endoscopy vans providing endoscopy, colonoscopy, and ultrasounds. To date, an estimated 20 million patients have been reached through this project and the mobile endoscopy van idea has been replicated in another state in India, Sikkim. There is an opportunity to replicate this concept in other states in India (e.g., Chhattisgarh) as well as in rural areas of other countries in order to make gastrointestinal care accessible to the poorest of the poor who cannot make their way to urban centers for diagnostic testing. Data from these mobile endoscopy vans can also be used to gauge the true incidence and prevalence of Crohn's disease.

## **Develop Crohn's disease registries**

ALL OF THE PROVIDERS we met with in India and Nepal expressed interest in participating in a multi-country registry of Crohn's disease. Both Rupa Banerjee at AIG and Vineet Ahuja at AIIMS have large cohorts of Crohn's disease patients they are actively collecting data on. They have both blood/plasma and tissue repositories for their patient cohorts. There is also some socioeconomic data collected in the form of "Occupation" and "Education level" of patients, and possibly whether or not they have a "Below the Poverty Line" card. Rupa Banerjee has established an Emerging Economies IBD database, which is soon to be online, that will include Crohn's cohorts from various countries in South Asia and the Middle East. Thus, there is an opportunity to study a large number of Crohn's patients in LLMICs through these established cohorts and databases. Our main interest in utilizing these registries would be in the context of monitoring expanded access to treatment and also to see if the poor are being reached, as well as to understand the population epidemiology of Crohn's.

PROVIDERS IN ALL THREE COUNTRIES we visited in Africa expressed interest in participating in a multi-country registry of Crohn's disease patients. This is particularly needed in Ethiopia, where Crohn's is being seen more and more, both to assist providers in diagnosing and caring for Crohn's patients, but also to conduct epidemiologic research on Crohn's disease in Ethiopia. This is a unique opportunity to study the burden of Crohn's where it is emerging, which is often when the most can be learned about the underlying causes of a disease, something that is still largely unknown when it comes to Crohn's. Dr. Haile and his colleagues at Saint Paul's Hospital have already begun to collect data on some of their own Crohn's disease patients, and Black Lion has a large cohort, both of which could be a great starting point for an Ethiopian- or African-wide Crohn's clinical registry. Ethiopia by far had the most Crohn's patients compared to

Malawi and Rwanda, which was surprising as this is not reflected in the literature. Further, the lack of published data on Crohn's disease in Ethiopia, despite its rising burden, suggests that countries lacking Crohn's disease data may be due to limited research capacity, rather than a true rarity of patients, and highlights the importance of population-based epidemiologic studies in these settings.

## **Provide pathology support**

ACCESS TO QUALITY PATHOLOGY services was mentioned as an issue by gastroenterologists in numerous countries, including Malawi, Ethiopia, and Nepal. Dr. Peter Finch, the only trained gastroenterologist in Malawi, explained that the high cost of histology is a major barrier to Crohn's disease patients obtaining an accurate diagnosis. He explained that most patients cannot afford histology and so it is not often used, and he has to rely on clinical diagnosis and what he sees visually on colonoscopy without tissue pathology. In Ethiopia, on the other hand, the issue was not cost of pathology as much as lack of a trained GI pathologist. Providers at Saint Paul's Hospital and Teklehamanot General Hospital are able to take biopsies and send them for histology, but the samples are analyzed by a general pathologist without specific training in gastrointestinal pathology. The same issue was mentioned by multiple doctors in Nepal as well. This may be an opportunity to train a GI pathologist, or to utilize telemedicine/telepathology services.

## **Increase Crohn's disease awareness among local gastroenterologists, internists and surgeons through Continuing Medical Education programs or conferences**

MANY OF THE GASTROENTEROLOGY providers from LLMICs in both our survey and site visits spoke of a lack of Crohn's disease awareness among local gastroenterologists and other medical providers. There was a general misunderstanding that diseases

like Crohn's did not exist in their countries and thus it was not even considered on a differential diagnosis of patients presenting with typical symptoms. It may be worthwhile to consider hosting a Crohn's or inflammatory bowel disease conference which would serve as a Continuing Medical Education conference for providers in these countries, particularly in Ethiopia where there appears to be an increasing burden of Crohn's patients.

### **Encourage and fund further research on distinguishing Crohn's disease from intestinal tuberculosis**

ALGORITHMS for accurately diagnosing Crohn's and intestinal TB is an important area of gastroenterology research in LLMICs. The most frequently reported challenge respondents face in diagnosing Crohn's disease in LLMICs is differentiating it from intestinal TB. While many providers use traditional methods such as imaging and AFB staining of biopsy samples, a large proportion will also empirically treat suspected cases with a course of anti-TB therapy, and only consider Crohn's if the patient does not respond. This can lead to significant delays in diagnosis and thus receiving appropriate treatment. In this context, there may be opportunities to take advantage of the use of Gene Xpert technology (perhaps on pathology samples) or in integration of TB and NCD laboratory platforms in both service delivery and financing.

### **Address the high cost of biologic therapies**

THE HIGH COST (\$1700 per dose of Infliximab in India) of biologic therapies for Crohn's disease was a major barrier to care of Crohn's disease in most LLMICs. A program to provide high-cost biologics to poor patients who desperately need them would be very useful at higher level referral centers with large numbers of Crohn's patients (e.g., AIIMS and AIG in India). In many LLMICs, biologics cannot even be obtained, even for the small number of patients who

could pay for them. The high cost and unavailability of biologics could be addressed via inclusion in essential medicine formularies, increased advocacy, collective demand creation and generic production.

### **Address the high costs of diagnostics**

PATIENTS' INABILITY to afford diagnostic testing is also a significant challenge. Upper endoscopies tend to be fairly affordable, but colonoscopies with biopsies and abdominal CT scans can be costly, which most substantially impacts patients of lower socio-economic status.

### **Fund research on the true epidemiology of Crohn's disease**

IT IS CLEAR from the discrepancies between our scoping review and the provider surveys that more Crohn's disease exists than is documented in the published literature. Even the published literature can be biased and may not reflect true prevalence estimates, which can only be obtained via community-based screening. For example, Vineet Ahuja and Saurabh Kedia are currently conducting an IBD epidemiology study in an area of Kolkata, through a partnership with a Public Health Institute. They are surveying people door to door for GI symptoms, carrying out fecal occult blood testing and if positive, checking a fecal calprotectin. If this is positive, they get more advanced work up including colonoscopies. Data collection is currently ongoing for this study. There is an opportunity to replicate this type of study in other areas of India, (e.g., rural Chhattisgarh) as part of the ongoing NCD project there or in other countries like Ethiopia where a strong signal for Crohn's is emerging.

### **Provide human resource support to the public sector in the form of gastroenterology specialists**

THE PUBLIC SECTOR in most LLMICs is generally weaker than the private sector. For example, Raipur in India lacks a gastroenterologist, although surgeons do perform endoscopic procedures. Private sector

gastroenterologists see most of the IBD and Crohn's disease patients in Raipur. Similarly, in Malawi, there is a single gastroenterologist in the whole country who is actually an expat. There may be opportunities to build up the public sector in LLMICs in terms of gastrointestinal and Crohn's disease care through human resource supports in the form of gastroenterology specialists.

### **Establish Crohn's disease support groups**

We were extremely impressed with the Crohn's patient and medical intern we met at Saint Paul's Hospital, and the work she is doing to support other patients with her illness in Ethiopia. There is a great opportunity to support the platform she is creating, as well as to help her to expand it outside Addis and potentially to other countries.

### **Encourage the collection of socioeconomic information in future studies**

Although Crohn's disease has historically been documented primarily among wealthier populations living in urban centers, our scoping review does indicate some signal of Crohn's in patients living in rural areas in India, Sri Lanka, Egypt, Tunisia, Ethiopia, Kenya, Indonesia, the Philippines, and Bolivia. In addition, most of our survey participants estimated that approximately 26-50% of their patients diagnosed with Crohn's live in rural areas (**Figure 11**). When stratified by region, Asian providers reported somewhat higher proportions of their patients living in rural areas. Future studies should collect and report data on the geography of where patients reside, as well as socioeconomic information such as income-level or employment.



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# Appendix

# Crohn's Disease

# Among the

# Poorest Billion

**Appendix 1.1.** Search strategy (PubMed)

Search	Query	Records retrieved
#1	("Crohn Disease"[Mesh] OR "Inflammatory Bowel Diseases"[Mesh] OR Crohn Disease[tiab] OR Crohns Disease[tiab] OR Crohn's Disease[tiab] OR Crohn's Enteritis[tiab] OR Crohns Enteritis[tiab] OR Regional Enteritis[tiab] OR Inflammatory Bowel Disease[tiab] OR Granulomatous Enteritis[tiab] OR Ileocolitis[tiab] OR Granulomatous Colitis[tiab] OR Terminal Ileitis[tiab] OR Regional Ileitides[tiab] OR Regional Ileitis[tiab] OR colonoscopy OR small bowel follow through[tiab] OR magnetic resonance enterography[tiab] OR small bowel enterography[tiab] OR barium enema[tiab] OR (transverse fissures AND (colon[tiab] OR bowel[tiab])) OR edema of the bowel[tiab] OR (intra-abdominal abscess[tiab] AND (colon[tiab] OR bowel[tiab])) OR (abdominal CT[tiab] AND ileitis[tiab]) OR stool calprotectin[tiab] OR fecal calprotectin[tiab] OR anti-saccharomyces cerevisiae antibodies[tiab] OR (ulcers[tiab] AND (colon[tiab] OR bowel[tiab])) OR (cobblestone [tiab] AND (colon[tiab] OR bowel[tiab])) OR (skip lesions[tiab] AND (colon[tiab] OR bowel[tiab])) OR (serpiginous[tiab] AND (colon[tiab] OR bowel[tiab])) OR (pseudopolyps[tiab] AND (colon[tiab] OR bowel[tiab])) OR (creeping fat[tiab] AND (colon[tiab] OR bowel[tiab])) OR small bowel stricture[tiab] OR ileal stricture[tiab] OR small bowel obstruction[tiab] OR ostomy[tiab] OR small bowel resection[tiab] OR colectomy[tiab] OR strictureplasty[tiab] OR ileoanal pouch[tiab] OR j pouch[tiab] OR enteric fistula[tiab] OR enterocutaneous fistula[tiab] OR (perianal fissure[tiab] AND (colon[tiab] OR bowel[tiab])) OR (perianal fistula AND (colon[tiab] OR bowel[tiab])) OR (transmural inflammation[tiab] AND (colon[tiab] OR bowel[tiab])) OR (granuloma*[tiab] AND (colon[tiab] OR bowel[tiab])) OR (cryptitis[tiab] AND (colon[tiab] OR bowel[tiab])) OR (crypt abscess[tiab] AND (colon[tiab] OR bowel[tiab])) OR (plasmacytosis[tiab] AND (colon[tiab] OR bowel [tiab])) OR (obliterative muscularization of submucosa[tiab] OR (sulfasalazine[tiab] AND (colon[tiab] OR bowel [tiab])) OR (mesalamine[tiab] AND (colon[tiab] OR bowel[tiab])) OR (budesonide[tiab] AND (colon[tiab] OR bowel [tiab])) OR (anti-TNF[tiab] AND (colon[tiab] OR bowel[tiab])) OR (infliximab[tiab] AND (colon[tiab] OR bowel[tiab])) OR (remicade[tiab] AND (colon[tiab] OR bowel[tiab])) OR (humira[tiab] AND (colon[tiab] OR bowel[tiab])) OR (immunomodulator AND (colon[tiab] OR bowel[tiab])) OR (methotrexate[tiab] AND (colon[tiab] OR bowel[tiab])) OR (asathiopurine[tiab] AND (colon[tiab] OR bowel[tiab])) OR (mercaptopurine[tiab] AND (colon[tiab] OR bowel[tiab]))	91,726
#2	("Developing Countries"[mesh] OR developing countr*[tiab] OR developing nation*[tiab] OR less developed countr*[tiab] OR less developed nation*[tiab] OR third world nation*[tiab] OR third world countr*[tiab] OR under developed nation*[tiab] OR underdeveloped nation*[tiab] OR under developed countr*[tiab] OR underdeveloped nation*[tiab] OR low income countr*[tiab] OR low income nation*[tiab] OR poor countr*[tiab] OR poor nation*[tiab] OR Imic[tiab] OR Imics[tiab] OR Afghanistan*[tiab] OR Angola*[tiab] OR Armenia*[tiab] OR Bangladesh*[tiab] OR Benin[tiab] OR Bhutan*[tiab] OR Bolivia*[tiab] OR Burkina Faso[tiab] OR Burundi*[tiab] OR Cabo Verd*[tiab] OR Cape Verd*[tiab] OR Cambodia*[tiab] OR Cameroon*[tiab] OR Central African*[tiab] OR Chad*[tiab] OR Comoros[tiab] OR Comores[tiab] OR Comores[tiab] OR Congo[tiab] OR Cote d Ivoire[tiab] OR Ivory Coast[tiab] OR Djibouti[tiab] OR Egypt*[tiab] OR El Salvador*[tiab] OR Eritrea*[tiab] OR Ethiopia*[tiab] OR Gambia*[tiab] OR Gaza[tiab] OR Georgia*[tiab] OR Ghana*[tiab] OR Guatemala*[tiab] OR Guinea*[tiab] OR Haiti*[tiab] OR Hondura*[tiab] OR India[tiab] OR Indian*[tiab] OR Indonesia*[tiab] OR Jordan[tiab] OR Kenya*[tiab] OR Kiribati[tiab] OR democratic people's republic of korea[tiab] OR North Korea[tiab] OR Kosovo[tiab] OR Kosovar*[tiab] OR Kyrgyz*[tiab] OR Kirghizia[tiab] OR Kirghiz[tiab] OR Kirgizstan[tiab] OR Lao[tiab] OR Laos[tiab] OR Laotian*[tiab] OR Lesotho[tiab] OR Liberia*[tiab] OR Madagascar*[tiab] OR Malawi*[tiab] OR Mali[tiab] OR Malian[tiab] OR Marshall Island*[tiab] OR Mauritania*[tiab] OR Mauriti*[tiab] OR Micronesia*[tiab] OR Micronesia*[tiab] OR Moldova*[tiab] OR Mongolia*[tiab] OR Morocc*[tiab] OR Mozambique [tiab] OR Myanmar[tiab] OR Burmese*[tiab] OR Burma[tiab] OR Nepal*[tiab] OR Nicaragua*[tiab] OR Niger*[tiab] OR Pakistan*[tiab] OR Palau[tiab] OR Papua New Guinea[tiab] OR Philippin*[tiab] OR Phillipin*[tiab] OR Philipin*[tiab] OR Phillipin*[tiab] OR Principe[tiab] OR Rwanda*[tiab] OR Ruanda*[tiab] OR Sao Tome[tiab] OR Senegal*[tiab] OR Sierra Leone*[tiab] OR Solomon Island*[tiab] OR Somalia*[tiab] OR South Sudan*[tiab] OR Sri Lanka[tiab] OR Sudan*[tiab] OR Swaziland*[tiab] OR Syria*[tiab] OR Tajik*[tiab] OR Tadjhik*[tiab] OR Tadjik*[tiab] OR Tanzania*[tiab] OR Timor*[tiab] OR Togo*[tiab] OR Tunisia*[tiab] OR Uganda*[tiab] OR Ukrain*[tiab] OR Uzbeki*[tiab] OR Vanuatu*[tiab] OR Vietnam*[tiab] OR Viet nam*[tiab] OR West Bank[tiab] OR Yemen*[tiab] OR Zambia*[tiab] OR Zimbabw*[tiab])	701,191
#3	#1 AND #2	1,699
	Limited to English language	1,575

**Appendix 1.2.** Data extraction instrument

Study #	Title/abstract review	Full text review	SS/RR reviewed	Corresponding author mail	Title	Conference abstract?	Authors	Authors Journal
Article type	Publication date	Country	Facility name	Facility type	Sub-National Region	Regional classification	World Bank country income level classification	
Important background info	Study years	Study objective	Study design	Study sample	Results	Conclusions	Limitations	

**IBD LLMIC Burden**

Number of cases	Prevalence	Incidence (risk)	Incidence rate	Odds	Mortality rate	DALY rate	Average disease duration
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**Crohn's LLMIC Burden**

Number of cases	Prevalence	Incidence (risk)	Incidence rate	Odds	Mortality rate	DALY rate	Average disease duration
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**Clinical features**

Age at diagnosis	Sex	Risk factors	Disease severity	Disease behavior	Disease location	Median CDAI	Extraintestinal manifestations	Comorbidities	Outcomes
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**Care pathways**

Diagnosis	Disease management	Long-term/follow-up car	Complications	Blood tests	Stool tests	Biopsy/tissue pathology	TB testing
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**Services Available**

**Services Available**

Endoscopy	Radiology/imaging	Medications	Surgeries	Equipment	Providers	Financing
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**Challenges and barriers**

Diagnostic challenges	Management challenges	Other provider challenges	Access barriers to patients	Financial barriers to patients	Other patient barriers
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**Patient demographics**

Age at time of study	Residency (urban vs rural)	SES characteristics	Insurance coverage	Out of pocket costs
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**Appendix 1.3.** Summary of all studies included in review by world region, country, World Bank income level, and year of publication

Region	#of studies (%*)	Country	#of studies (%*)
South Asia	129 (59.7)	India	107 (49.5)
		Sri Lanka	11 (5.1)
		Pakistan	9 (4.2)
		Nepal	9 (4.2)
		Bangladesh	2 (0.9)
Middle East & North Africa	67 (31.0)	Tunisia	41 (19.0)
		Egypt	18 (8.3) †
		Morocco	7 (3.2)
		Syria	1 (0.5)
sub-Saharan Africa	16 (7.4)	Nigeria	5 (2.3)
		Sudan	3 (1.4)
		Ethiopia	2 (0.9)
		Kenya	2 (0.9)
		Uganda	1 (0.5)
		Cameroon	1 (0.5)
		Ghana	1 (0.5)
		Malawi	1 (0.5)
East Asia & Pacific	5 (2.3)	Indonesia	3 (1.4)
		Philippines	2 (0.9)
		Vietnam	1 (0.5)
Latin America & the Caribbean	1 (0.5)	Bolivia	1 (0.5)
<b>Income level</b>		<b>#of studies (%)</b>	
Low income	8 (3.7)		
Lower middle income	208 (96.3)		
<b>Publication year</b>		<b>#of studies (%)</b>	
Before 1970	1 (0.5)		
1970-1979	5 (2.3)		
1980-1989	8 (3.7)		
1990-1999	8 (3.7)		
2000-2009	52 (24.1)		
2010-2019	142 (65.7)		

\*Number of studies do not add up to exactly 100% due to 3 multi-country studies that included countries in both South Asia and East Asia & Pacific

†Countries that do not have any published IBD studies, but have published articles that describe diagnostics or findings associated with IBD



**Appendix 1.4.** Number of studies reporting utilization of Crohn's disease diagnostic and treatment services by region and country

Region/Country	Diagnostic								Medical						Surgical						
	Endoscopy	Pathology	Radiology	Blood Testing	Stool Testing	TB Testing	Trial of ATT disc used	Surgical/autopsy diagnosis	Clinical diagnosis	Corticosteroids	Aminosalicyclates	Immunomodulators	Biologics	Nutritional therapy	Colectomy	Ostomy	Small bowel resection	Ileanal pouch	Strictureplasty	Unspecified surgery	Other
<b>Overall (N=216)</b>	<b>112</b>	<b>110</b>	<b>109</b>	<b>117</b>	<b>75</b>	<b>45</b>	<b>15</b>	<b>12</b>	<b>2</b>	<b>77</b>	<b>66</b>	<b>54</b>	<b>26</b>	<b>6</b>	<b>26</b>	<b>6</b>	<b>23</b>	<b>-</b>	<b>5</b>	<b>26</b>	<b>36</b>
<b>South Asia (N=129)</b>	<b>74</b>	<b>66</b>	<b>64</b>	<b>58</b>	<b>37</b>	<b>42</b>	<b>13</b>	<b>6</b>	<b>1</b>	<b>49</b>	<b>40</b>	<b>41</b>	<b>22</b>	<b>4</b>	<b>17</b>	<b>5</b>	<b>13</b>	<b>-</b>	<b>4</b>	<b>15</b>	<b>26</b>
India (N=107)	57	50	50	51	32	37	11	5	-	39	36	36	17	4	12	3	11	-	3	13	20
Sri Lanka (N=11)	7	4	4	3	2	2	-	-	-	5	2	3	3	-	2	1	-	-	-	1	1
Pakistan (N=9)	8	7	5	3	2	1	2	-	-	4	2	2	1	-	2	1	1	-	1	-	2
Nepal (N=3)	2	3	3	1	-	-	-	1	-	1	-	1	1	-	1	-	1	-	-	-	2
Bangladesh (N=2)	-	2	2	-	1	2	-	-	1	-	-	-	-	-	-	-	-	-	-	1	1
<b>Middle East &amp; North Africa (N=67)</b>	<b>22</b>	<b>29</b>	<b>32</b>	<b>48</b>	<b>12</b>	<b>1</b>	<b>-</b>	<b>3</b>	<b>-</b>	<b>20</b>	<b>18</b>	<b>11</b>	<b>4</b>	<b>1</b>	<b>7</b>	<b>-</b>	<b>6</b>	<b>-</b>	<b>1</b>	<b>11</b>	<b>4</b>
Tunisia (N=41)	24	15	17	30	2	-	-	2	-	15	13	8	3	-	5	-	5	-	1	10	1
Egypt (N=18)	15	12	12	14	9	1	-	1	-	5	5	3	1	1	2	-	1	-	-	-	2
Morocco (N=7)	5	2	3	4	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	1
<b>sub-Saharan Africa (N=16)</b>	<b>11</b>	<b>12</b>	<b>10</b>	<b>11</b>	<b>9</b>	<b>2</b>	<b>2</b>	<b>3</b>	<b>1</b>	<b>7</b>	<b>6</b>	<b>2</b>	<b>-</b>	<b>1</b>	<b>1</b>	<b>1</b>	<b>3</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>7</b>
Nigeri (N=5)	3	4	3	4	4	-	-	-	1	4	3	-	-	-	-	-	1	-	-	-	2
Sudan (N=3)	2	2	2	1	1	1	-	1	-	1	1	-	-	-	-	-	-	-	-	-	1
Ethiopia (N=2)	2	2	2	2	1	-	1	1	-	1	1	-	-	-	1	-	1	-	-	-	2
Kenya (N=2)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1
Uganda (N=1)	-	1	-	1	1	-	-	1	-	-	-	-	-	-	-	-	1	-	-	-	-
Ghana (N=1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Cameroon (N=1)	1	-	1	1	-	1	-	-	-	-	1	1	-	-	-	1	-	-	-	-	1
Malawi (N=1)	1	1	1	1	1	-	1	-	-	1	-	1	-	1	-	-	-	-	-	-	-
<b>East Asia &amp; Pacific (N=5)</b>	<b>5</b>	<b>3</b>	<b>3</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>1</b>	<b>2</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>1</b>	<b>-</b>	<b>1</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>1</b>
Indonesia (N=3)	3	2	3	-	-	-	-	-	-	-	1	-	-	-	-	-	1	-	-	-	1
Philippines (N=2)	1	-	-	-	-	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-
Vietnam (N=1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	1	-	-	-	-	-	-

\*Studies from Bolivia and Syria did not report on diagnostic or treatment services availability.

†Other surgeries include: anastomosis, unspecified anal surgery, and laparotomy

Number of studies do not add up to exactly 100% due to 3 multi-country studies that included countries in both South Asia and East Asia & Pacific.

**Appendix 1.5..** Summary of patient geographic residency, socioeconomic characteristics, insurance coverage, and out of pocket cost by region and country

Region/ Country	Study	Geography		Socio-economic conditions			Cost to patients
		Urban	Rural	Lower	Middle	Upper	
South Asia India	Blatt 2009				Mostly middle and upper SES	Mostly middle and upper SES	IBD: cost of medications not a factor - most patients middle and upper SES
						Mostly middle and upper SES	IBD: cost of medications not a factor - most patients middle and upper SES
	Singh 2010	Patients from cities					
	Balasubramanian 2011	in and around city					
	Pugazhendi 2011	126 (63.0%)	74 (37.0%)		Median SES score (possible range 3-28): 22 (IQR 18-26)	Median SES score (possible range 3-28): 22 (IQR 18-26)- higher in those with CD than	
	Makharia 2012	Most Urban					
	Goel 2013	135 (60.5%)	88 (39.5%)				
	Larsson 2014	More CD patients	More ITB patients	ITB: lower income and education		CD: higher income and education	
	Kamat 2017						15 (605) private insurance; 10 (405) uninsured
	Tomar 2017				IBD: 98 (31.0%) high school education	IBD: 97 (30.7%) college education	
	Amarapurkar 2018	239 (82.7%)	50 (17.3%)	118 (62.6%) nongraduates; 180 (62.3%) unemployed/unskilled; 242 (83.8%) annual family income <10000000 INR		108 (37.4%) graduates; 109 (37.7%) professional occupation; 47 (16.2%) annual family income >10000000	
	NG 2018*	Both	Both				
Kamat 2019	Both	Both				IBD: 14.3% discontinued Adalimumab due to high cost	

<b>Sri Lanka</b>	Subasinghe 2010	IBD: 48 (26.1%)	IBD: 136 (73.9%)			
	NG 2016*	Urban				
	NG 2018*	Both		Both		
<b>Middle East &amp; North Africa</b>						
	Egypt	Esmat 2014	21 (95.5%)	1 (4.5%)		
Tunisia		Hadrich 2007	19 (48.7%)			
		Ennaifer 2014		IBD: 3 (5%) had no education	IBD: 10 (49%) had primary education, 16 (26.6%) had secondary education	IBD: 31 (51.6%) had university education
		Mrabet 2017	ITB: 37 (34.3% "bad" SES; 84 (77.8%) illiterate/primary/secondary education; 46 (42.6%) no employment	ITB: 53 (49) "good" SES; 84 (77.8%) illiterate/primary/secondary education; 62 (57.4%) employed/	IBD:18 (16.7%) "well" SES; 24 (22.2%) university education; 62 (57.4%) employed/student	
		Sahli 2018	IBD 45 (70.3%)	IBD 19 (29.7%)		
<b>sub-Saharan Africa</b>						
	Nigeria	Alatise 2012			National Health Insurance Schemes available but does not cover majority of people and does not cover chronic diseases- treatments paid for out of pocket	
		Ekwunife 2015			Cost for medications that incurred paid by patients themselves	
Ethiopia	Mengesha 1997	6 (85.7%)	1 (14.3%)			
Kenya	Steury 1980	1				
Sudan	Khalifa 2005		4 (33%) low	8 (67%) high/middle	8 (67%) high/middle	



<b>East Asia &amp; Pacific</b>	Indonesia	NG 2016*	Urban	
		NG 2018*	Both	Both
	Philippines	NG 2018*	Both	Both
<b>Latin America &amp; the Caribbean</b>	Bolivia	Rois-Dalenz 1975		Many patients rural

**Appendix 1.6.** Summary of diagnostic, management, access, and financial challenges and barriers to CD patients and providers in LLMICs

Diagnostic Challenges	Country (#of studies)	Total # of studies
Difficulty differentiating between CD and ITB	India (23), Nigeria (3), Sri Lanka (1), Bangladesh (1), Ethiopia (2), Kenya (1), Pakistan (1), Uganda (1), Sudan (2)	36
Low disease index of suspicion/clinical awareness due to perceived rarity of CD leads to underdiagnosis	Nigeria (5), India (4), Egypt (2), Sri Lanka (1), Ghana (1), Bolivia (1) Ethiopia (1), Sri Lanka (2),	17
Difficulty differentiating between CD and other infectious diseases	Egypt (5), India (6), Nigeria (1), Sri Lanka (1) Kenya (1), Tunisia (1), Pakistan (1)	16
Lack of quality diagnostic facilities and investigational modalities	India (4), Nigeria (1), Egypt (3), Bangladesh (1), Nepal (1), Cameroon (1), Kenya (1), Indonesia (2)	14
Lack of reliable TB testing modalities	India (1), Sri Lanka (1)	2
Difficulty differentiating between CD and UC	India (3), Nepal (1), Nigeria (1), Tunisia (1), Pakistan (1)	7
Diagnosis of CD made on histological exam of resected colon	India (1), Tunisia (1)	3
<b>Management Challenges</b>		
Use of biologics is limited to cost	India (3)	3
High risk of TB infection reactivation in patients treated with biologics	India (1)	1
<b>Access Barriers</b>		
Lack of access to high quality health care services	India (1), Nepal (1), Bangladesh (1)	3
Lack of access to CD medications	Nigeria (1)	1
Lack of education/knowledge about disease	India (3), Tunisia (1), Sri Lanka (1)	3
<b>Financial Barriers</b>		
Patients unable to afford biologics	India (3)	3
Patients unable to afford treatment in general (medications and surgeries)	India (3), Egypt (2), Sri Lanka (1), Pakistan (1), Ghana (1), Nigeria (1)	9
Lack of insurance coverage	India (3), Nigeria (1)	4
High cost of diagnostic testing	India (2), Sri Lanka (1), Egypt (1)	4

**Table 2.1.** Survey respondent demographic characteristics overall and by country

	Country															
	Overall	India	Ethiopia	Nepal	Egypt	Nigeria	Indonesia	Malawi	Pakistan	Rwanda	Bangladesh	Kenya	Philippines	Sudan	Tunisia	Zimbabwe
<b>N</b>	<b>46</b>	10 (21.7)	8 (17.4)	6 (13.0)	4 (8.7)	3 (6.5)	2 (4.3)	2 (4.3)	2 (4.3)	2 (4.4)	1 (2.2)	1 (2.2)	1 (2.2)	2 (4.3)	1 (2.2)	1 (2.2)
<b>Age group in years</b>																
<25	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
25-34	3 (6.5)	-	3 (37.5)	-	-	-	-	-	-	-	-	-	-	-	-	-
35-44	15 (32.6)	2 (20.0)	5 (62.5)	2 (33.3)	1 (25.0)	-	-	-	2 (100.0)	-	-	1 (100.0)	-	1 (50.0)	1 (100.0)	1 (100.0)
45-54	12 (26.1)	1 (10.0)	-	4 (66.7)	3 (75.0)	3 (100.0)	-	1 (50.0)	-	-	-	-	-	-	-	-
55-64	7 (15.2)	1 (10.0)	-	-	-	-	2 (100.0)	1 (50.0)	-	2 (100.0)	-	-	1 (100.0)	-	-	-
>65	3 (6.25)	2 (20.0)	-	-	-	-	-	-	-	-	1 (100.0)	-	-	-	-	-
Missing	6 (13.0)	4 (40.0)	-	-	-	-	-	-	-	-	-	-	-	1 (50.0)	-	-
<b>Gender</b>																
Male	37 (80.4)	8 (80.0)	6 (75.0)	6 (100.0)	4 (100.0)	2 (66.7)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	1 (100.0)	1 (100.0)	-	-	-	1 (100.0)
Female	7 (15.2)	1 (10.0)	2 (25.0)	-	-	1 (33.3)	-	-	-	-	-	-	1 (100.0)	1 (50.0)	1 (100.0)	-
Missing	2 (4.3)	1 (10.0)	-	-	-	-	-	-	-	-	-	-	-	1 (50.0)	-	-
<b>Level of training</b>																
MD/DO	38 (82.6)	8 (80.0)	7 (87.5)	6 (100.0)	4 (100.0)	2 (66.7)	1 (50.0)	2 (100.0)	1 (50.0)	1 (50.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (50.0)	1 (100.0)	1 (100.0)
MBBS	3 (6.5)	-	-	-	-	1 (33.3)	-	-	1 (50.0)	-	-	-	-	-	-	-
Other	2 (4.3)	1 (10.0)	1 (12.5)	-	-	-	-	-	-	-	-	-	-	-	-	-
Missing	3 (6.5)	1 (10.0)	-	-	-	-	-	-	-	-	-	-	-	1 (50.0)	-	-
<b>Formal gastroenterology training:</b>																
Yes	40 (87.0)	9 (90.0)	7 (87.5)	6 (100.0)	4 (100.0)	3 (100.0)	2 (100.0)	1 (5.0)	2 (100.0)	1 (50.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (50.0)	-	1 (100.0)
No	3 (6.5)	-	1 (12.5)	-	-	-	-	1 (50.0)	-	-	-	-	-	-	1 (100.0)	-
Missing	3 (6.5)	1 (10.0)	-	-	-	-	-	-	-	1 (50.0)	-	-	-	1 (50.0)	1 (100.0)	-
<b>Formal gastroenterology training:</b>																
1	5 (10.9)	-	-	3 (50.0)	-	2 (66.7)	-	-	-	-	-	-	-	-	-	-
2	12 (26.1)	-	7 (87.5)	-	2 (50.0)	-	-	-	-	1 (50.0)	-	1 (100.0)	-	1 (50.0)	-	-
3	10 (21.7)	4 (40.0)	-	2 (33.3)	-	-	-	-	2 (100.0)	-	-	1 (100.0)	-	-	-	1 (100.0)
>4	9 (19.6)	2 (20.0)	-	1 (16.7)	2 (50.0)	1 (33.3)	2 (100.0)	-	-	-	1 (100.0)	-	-	-	-	-
Missing	10 (21.7)	4 (40.0)	1 (12.5)	-	-	-	-	2 (100.0)	-	1 (50.0)	-	-	-	1 (50.0)	1 (100.0)	-

**Table 2.2.** Typical duration of symptoms for patients diagnosed with Crohn's in LLMICs

Country	Number of months				Missing
	<6	6 to 12	12 to 24	>24	
<b>Overall</b>	<b>2 (4.3)</b>	<b>18 (39.1)</b>	<b>10 (21.7)</b>	<b>6 (13.0)</b>	<b>10 (21.7)</b>
<b>Asia (N=46)</b>	1 (4.5)	10 (45.5)	4 (18.2)	2 (9.1)	5 (22.7)
India (N=10)	-	2 (20.0)	3 (30.0)	1 (10.0)	4 (40.0)
Nepal (N=6)	-	4 (66.7)	-	1 (16.7)	1 (16.7)
Indonesia (N=2)	-	2 (100.0)	-	-	-
Pakistan (N=2)	-	2 (100.0)	-	-	-
Bangladesh (N=1)	-	-	1 (100.0)	-	-
Philippines (N=1)	1 (100.0)	-	-	-	-
<b>Africa (N=24)</b>	1 (4.2)	8 (33.3)	6 (25.0)	4 (16.7)	5 (20.8)
Ethiopia (N=8)	-	4 (50.0)	2 (25.0)	2 (25.0)	-
Egypt (N=4)	-	3 (75.0)	1 (25.0)	-	-
Nigeri (N=3)	1 (33.3)	-	1 (33.3)	1 (33.3)	-
Malawi (N=2)	-	-	1 (50.0)	-	1 (50.0)
Rwanda (N=2)	-	-	-	-	2 (100.0)
Sudan (N=2)	-	-	-	-	2 (100.0)
Kenya (N=1)	-	-	1 (100.0)	-	-
Tunisia (N=1)	-	1 (100.0)	-	-	-
Zimbabwe (N=1)	-	-	-	1 (100.0)	-



**Table 2.3.** Availability of diagnostic technology involved in diagnosing Crohn's disease

	Laboratory testing										
	Tissue pathology from biopsies	Erythrocyte sedimentation rate (ESR)	C-Reactive protein (CRP)	Thiopurine methyltransferase (TPMT)	Stool calprotectin	Tuberculin skin test (Mantoux test)	Staining for acid-fast bacilli (AFB)	Mycobacterium tuberculosis (MTB) culture)	TB-P CR	IGRA (T-spot)	Hep B surface antigen test
<b>Overall N=44*</b>	<b>44 (100.0)</b>	<b>44 (100.0)</b>	<b>43 (97.7)</b>	<b>13 (29.5)</b>	<b>33 (75.0)</b>	<b>36 (81.8)</b>	<b>44 (100.0)</b>	<b>38 (86.4)</b>	<b>41 (93.2)</b>	<b>23 (52.3)</b>	<b>41 (93.2)</b>
<b>Asia N=21*</b>	<b>21 (100.0)</b>	<b>21 (100.0)</b>	<b>21 (100.0)</b>	<b>12 (57.1)</b>	<b>21 (100.0)</b>	<b>21 (100.0)</b>	<b>21 (100.0)</b>	<b>19 (90.5)</b>	<b>21 (100.0)</b>	<b>19 (90.5)</b>	<b>19 (90.5)</b>
India N=9*	9 (100.0)	9 (100.0)	9 (100.0)	8 (88.9)	9 (100.0)	9 (100.0)	9 (100.0)	9 (100.0)	9 (100.0)	9 (100.0)	9 (100.0)
Nepal N=6*	6 (100.0)	6 (100.0)	6 (100.0)	3 (50.0)	6 (100.0)	6 (100.0)	6 (100.0)	5 (83.3)	6 (100.0)	4 (66.7)	4 (66.7)
Indonesia N=2*	2 (100.0)	2 (100.0)	2 (100.0)	-	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)
Pakistan (N=2)	2 (100.0)	2 (100.0)	2 (100.0)	1 (50.0)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)
Bangladesh (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	-	1 (100.0)	1 (100.0)	1 (100.0)	-	1 (100.0)	1 (100.0)	1 (100.0)
Philippines (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	-	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)
<b>Africa (N=23)</b>	<b>23 (100.0)</b>	<b>23 (100.0)</b>	<b>22 (95.7)</b>	<b>1 (4.3)</b>	<b>12 (52.2)</b>	<b>15 (65.2)</b>	<b>23 (100.0)</b>	<b>19 (82.6)</b>	<b>20 (87.0)</b>	<b>4 (17.4)</b>	<b>22 (95.7)</b>
Ethiopia (N=8)	8 (100.0)	8 (100.0)	8 (100.0)	-	2 (25.0)	1 (12.5)	8 (100.0)	8 (100.0)	7 (87.5)	-	8 (100.0)
Egypt (N=4)	4 (100.0)	4 (100.0)	4 (100.0)	-	4 (100.0)	4 (100.0)	4 (100.0)	2 (66.7)	4 (100.0)	1 (2.5)	4 (100.0)
Nigeria (N=3)	3 (100.0)	3 (100.0)	3 (100.0)	-	2 (66.7)	3 (100.0)	3 (100.0)	2 (66.7)	2 (66.7)	-	3 (100.0)
Malawi (N=2)	2 (100.0)	2 (100.0)	1 (50.0)	-	-	1 (50.0)	2 (100.0)	2 (100.0)	2 (100.0)	-	2 (100.0)
Rwanda (N=2)	2 (100.0)	2 (100.0)	2 (100.0)	-	-	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	-	1 (50.0)
Kenya (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	-	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)
Sudan (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	-	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	-	1 (100.0)
Tunisia (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)
Zimbabwe (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)
Endoscopy											
	Upper endoscopy	Colonoscopy	Video capsule endoscopy	Push enteroscopy	Double balloon enteroscopy	Ultrasound endoscopy	PEG				
<b>Overall N=44*</b>	<b>43 (97.7)</b>	<b>43 (97.7)</b>	<b>18 (40.9)</b>	<b>18 (40.9)</b>	<b>20 (45.5)</b>	<b>30 (68.2)</b>	<b>35 (79.5)</b>				
<b>Asia N=21*</b>	<b>21 (100.0)</b>	<b>21 (100.0)</b>	<b>14 (66.7)</b>	<b>15 (71.4)</b>	<b>17 (81.0)</b>	<b>21 (100.0)</b>	<b>21 (100.0)</b>				
India (N=9)*	9 (100.0)	9 (100.0)	7 (77.8)	8 (88.9)	7 (77.8)	9 (100.0)	9 (100.0)				
Nepal (N=6)	6 (100.0)	6 (100.0)	2 (33.3)	2 (33.3)	4 (66.7)	6 (100.0)	6 (100.0)				
Indonesia (N=2)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)				
Pakistan (N=2)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)				
Bangladesh (N=1)	1 (100.0)	1 (100.0)	-	-	1 (100.0)	1 (100.0)	1 (100.0)				
Philippines (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)				

<b>Africa N=23*</b>	<b>22 (95.7)</b>	<b>22 (95.7)</b>	<b>4 (17.4)</b>	<b>3 (13.0)</b>	<b>3 (13.0)</b>	<b>9 (39.1)</b>	<b>14 (60.9)</b>
Ethiopia (N=8)	8 (100.0)	8 (100.0)	-	-	-	2 (25.0)	2 (25.0)
Egypt (N=4)	4 (100.0)	4 (100.0)	-	1 (25.0)	-	4 (100.0)	4 (100.0)
Nigeria (N=3)	2 (66.7)	2 (66.7)	1 (33.3)	1 (33.3)	3 (100.0)	-	3 (100.0)
Malawi (N=2)	2 (100.0)	2 (100.0)	1 (50.0)	-	-	-	-
Rwanda (N=2)	2 (100.0)	-	-	-	-	-	2 (100.0)
Kenya (N=1)	1 (100.0)	1 (100.0)	-	-	-	1 (100.0)	1 (100.0)
Sudan (N=1)	1 (100.0)	1 (100.0)	-	-	-	1 (100.0)	1 (100.0)
Tunisia (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	-	-	1 (100.0)	-
Zimbabwe (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	-	-	1 (100.0)

### Radiology/Imaging

	X-Ray	Small bowel follow-through	Barium enema	Abdominal CT	CT enterography	MR enterography
<b>Overall N=44*</b>	<b>43 (97.7)</b>	<b>40 (90.9)</b>	<b>41 (93.2)</b>	<b>44 (100.0)</b>	<b>32 (72.7)</b>	<b>24 (54.5)</b>
<b>Asia N=21*</b>	<b>21 (100.0)</b>	<b>21 (100.0)</b>	<b>19 (90.5)</b>	<b>21 (100.0)</b>	<b>20 (95.2)</b>	<b>16 (76.2)</b>
India (N=9)*	9 (100.0)	9 (100.0)	9 (100.0)	9 (100.0)	9 (100.0)	9 (100.0)
Nepal (N=6)	6 (100.0)	6 (100.0)	6 (100.0)	6 (100.0)	6 (100.0)	4 (66.7)
Indonesia (N=2)	2 (100.0)	2 (100.0)	-	2 (100.0)	2 (100.0)	-
Pakistan (N=2)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	1 (50.0)	1 (50.0)
Bangladesh (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (50.0)
Philippines (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)
<b>Africa N=23*</b>	<b>23 (100.0)</b>	<b>19 (82.6)</b>	<b>22 (95.7)</b>	<b>23 (100.0)</b>	<b>12 (52.2)</b>	<b>8 (34.8)</b>
Ethiopia (N=8)	8 (100.0)	7 (87.5)	7 (87.5)	8 (100.0)	4 (50.0)	3 (37.5)
Egypt (N=4)	4 (100.0)	4 (100.0)	4 (100.0)	4 (100.0)	3 (75.0)	2 (50.0)
Nigeria (N=3)	3 (100.0)	2 (66.7)	3 (100.0)	3 (100.0)	3 (100.0)	2 (66.7)
Malawi (N=2)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	-	-
Rwanda (N=2)	2 (100.0)	-	2 (100.0)	2 (100.0)	-	-
Kenya (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	-	-
Sudan (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	-
Tunisia (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)
Zimbabwe (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	-	-

\*One missing response from Sudan and one missing response from India excluded.  
All values presented as mean (percent)

**Table 2.4.** How providers in LLMICs differentiate between Crohn's disease and Intestinal Tuberculosis

	Differentiation method				
	Imaging	AFB stain of biopsy samples	AFB stain of biopsy samples PCR of biopsy samples	Empirically treat TB first	Other
<b>Overall N=44*</b>	<b>26 (59.1)</b>	<b>24 (54.5)</b>	<b>19 (43.2)</b>	<b>22 (50.0)</b>	<b>8 (18.2)</b>
<b>Asia N=21*</b>	<b>13 (61.9)</b>	<b>11 (52.4)</b>	<b>12 (57.1)</b>	<b>13 (61.9)</b>	<b>4 (19.0)</b>
India(N=9)*	7 (77.8)	5 (55.6)	6 (66.7)	5 (55.6)	2 (22.2)
Nepal (N=6)	3 (50.0)	2 (33.3)	2 (33.3)	5 (83.3)	-
Indonesia (N=2)	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)
Pakistan (N=2)	1 (50.0)	2 (100.0)	2 (100.0)	1 (50.0)	-
Bangladesh (N=1)	1 (100.0)	-	-	1 (100.0)	1 (100.0)
Philippines (N=1)	-	1 (100.0)	1 (100.0)	-	-
<b>Africa N=23*</b>	<b>13 (56.5)</b>	<b>13 (56.5)</b>	<b>7 (30.4)</b>	<b>9 (39.1)</b>	<b>4 (17.4)</b>
Ethiopia (N=8)	6 (75.0)	4 (50.0)	2 (25.0)	7 (87.5)	2 (25.0)
Egypt (N=4)	2 (50.0)	4 (100.0)	1 (25.0)	-	-
Nigeria (N=3)	2 (100.0)	3 (100.0)	-	-	-
Malawi (N=2)	-	-	1 (50.0)	-	-
Rwanda (N=2)	-	-	-	-	2 (100.0)
Kenya (N=1)	-	1 (100.0)	1 (100.0)	-	-
Sudan (N=1)	1 (100.0)	-	1 (100.0)	1 (100.0)	-
Tunisia (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	-	-
Zimbabwe (N=1)	1 (100.0)	-	-	1 (100.0)	-

\*One missing response from Sudan and one missing response from India excluded | All values presented as mean (percent)

**Table 2.5.** Challenges faces by providers in LLMICs in diagnosing Crohn's disease

	Diagnostic challenges										
	Distinguishing between Crohn's and ITB	Distinguishing between Crohn's and other infectious diseases	Distinguishing between Crohn's and UC	Lack of access to diagnostic testing and imaging facilities	Poor quality of diagnostic facilities	Patients unable to afford the costs of diagnostic testing and imaging	Poor Crohn's disease awareness among providers	Lack of trained gastro-enterologists	Lack of trained path-ologists	Lack of reliable TB testing modalities	Other
<b>Overall N=44*</b>	<b>31 (70.5)</b>	<b>24 (54.5)</b>	<b>10 (22.7)</b>	<b>11 (25)</b>	<b>14 (31.8)</b>	<b>25 (56.8)</b>	<b>21 (47.7)</b>	<b>5 (11.4)</b>	<b>16 (36.4)</b>	<b>9 (20.5)</b>	<b>2 (4.5)</b>
<b>Asia N=21*</b>	<b>19 (90.5)</b>	<b>12 (57.1)</b>	<b>2 (9.5)</b>	<b>3 (14.3)</b>	<b>4 (19.0)</b>	<b>11 (52.4)</b>	<b>7 (33.3)</b>	<b>1 (4.8)</b>	<b>4 (19.0)</b>	<b>2 (9.5)</b>	<b>1 (4.8)</b>
India N=9*	8 (88.9)	6 (66.7)	-	-	1 (11.1)	5 (55.6)	2 (22.2)	-	1 (11.1)	1 (11.1)	1 (11.1)
Nepal N=6*	6 (100.0)	2 (33.3)	-	1 (16.7)	2 (33.3)	3 (50.0)	1 (16.7)	-	2 (33.3)	1 (16.7)	-
Indonesia N=2*	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)	-	-
Pakistan (N=2)	2 (100.0)	2 (100.0)	-	-	-	1 (50.0)	1 (50.0)	-	-	-	-
Bangladesh (N=1)	1 (100.0)	-	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	-	1 (100.0)	1 (100.0)	-
Philippines (N=1)	1 (100.0)	1 (100.0)	-	-	-	-	1 (100.0)	-	-	-	-
<b>Africa (N=23)</b>	<b>12 (52.2)</b>	<b>12 (52.2)</b>	<b>8 (34.8)</b>	<b>8 (34.8)</b>	<b>10 (43.5)</b>	<b>14 (60.9)</b>	<b>14 (60.9)</b>	<b>4 (17.4)</b>	<b>12 (52.2)</b>	<b>7 (30.4)</b>	<b>1 (4.3)</b>
Ethiopia (N=8)	8 (100.0)	7 (87.5)	4 (50.0)	3 (37.5)	6 (75.0)	6 (75.0)	6 (75.0)	2 (25.0)	6 (75.0)	4 (50.0)	1 (12.5)
Egypt (N=4)	-	-	1 (25)	-	-	2 (50.0)	3 (75.0)	-	1 (25.0)	1 (25.0)	-
Malawi (N=2)	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)	-	1 (50.0)	1 (50.0)	-	-
Nigeria (N=3)	-	1 (33.3)	-	-	1 (33.3)	3 (100.0)	2 (100.0)	1 (33.3)	1 (33.3)	-	-
Rwanda (N=2)	-	2 (100.0)	-	2 (66.7)	-	-	-	-	2 (100.0)	-	-
Kenya (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	-	1 (100.0)	-	-	-	-	-	-
Sudan (N=1)	1 (100.0)	-	-	1 (100.0)	1 (100.0)	1 (100.0)	-	-	1 (100.0)	-	-
Tunisia (N=1)	-	-	1 (100.0)	1 (100.0)	-	-	-	-	-	1 (100.0)	-
Zimbabwe (N=1)	1 (100.0)	1 (100.0)	-	-	-	1 (100.0)	1 (100.0)	-	-	1 (100.0)	-

\*One missing response from Sudan and one missing response from India excluded | All values presented as mean (percent)

**Table 2.6.** Availability of medications and surgeries for managing Crohn's in LLMICs overall, by region, and by country

	Aminosalicylates			
	Balsalazide	Mesalamine	Olsalazine	Sulfasalazine
<b>Overall N=44*</b>	<b>3 (6-8)</b>	<b>34 (77-3)</b>	<b>2 (4-5)</b>	<b>31 (70-5)</b>
<b>Asia N=21*</b>	<b>3 (14-3)</b>	<b>20 (95-2)</b>	<b>2 (9-5)</b>	<b>20 (95-2)</b>
India (N=9)*	2 (22-2)	9 (100-0)	1 (11-1)	9 (100-0)
Nepal (N=6)	1 (16-7)	6 (100-0)	-	6 (100-0)
Indonesia (N=2)	-	1 (50-0)	-	1 (50-0)
Pakistan (N=2)	-	2 (100-0)	-	2 (100-0)
Bangladesh (N=1)	-	1 (100-0)	-	1 (100-0)
Philippines (N=1)	-	1 (100-0)	1 (100-0)	1 (100-0)
<b>Africa N=23*</b>	<b>-</b>	<b>14 (60-9)</b>	<b>-</b>	<b>11 (47-8)</b>
Ethiopia (N=8)	-	2 (25-0)	-	1 (12-5)
Egypt (N=4)	-	4 (100-0)	-	4 (100-0)
Nigeria (N=3)	-	2 (66-7)	-	2 (100-0)
Malawi (N=2)	-	-	-	-
Rwanda (N=2)	-	2 (100-0)	-	-
Kenya (N=1)	-	1 (100-0)	-	1 (100-0)
Sudan (N=1)	-	1 (100-0)	-	1 (100-0)
Tunisia (N=1)	-	1 (100-0)	-	1 (100-0)
Zimbabwe (N=1)	-	1 (100-0)	-	1 (100-0)
	Corticosteroids			
	Budesonide	Methylprednisolone	Prednisolone	Prednisone
<b>Overall N=44*</b>	<b>21 (47-7)</b>	<b>30 (68-2)</b>	<b>43 (97-7)</b>	<b>24 (54-5)</b>
<b>Asia N=21*</b>	<b>20 (95-2)</b>	<b>20 (95-2)</b>	<b>20 (95-2)</b>	<b>15 (71-4)</b>
India (N=9)*	9 (100-0)	9 (100-0)	9 (100-0)	4 (66-7)
Nepal (N=6)	5 (83-3)	5 (83-3)	6 (100-0)	6 (100-0)
Indonesia (N=2)	2 (100-0)	2 (100-0)	2 (100-0)	2 (100-0)
Pakistan (N=2)	2 (100-0)	2 (100-0)	1 (50-0)	2 (100-0)
Bangladesh (N=1)	1 (100-0)	1 (100-0)	1 (100-0)	-
Philippines (N=1)	1 (100-0)	1 (100-0)	1 (100-0)	1 (100-0)
<b>Africa N=23*</b>	<b>1 (4-3)</b>	<b>10 (43-5)</b>	<b>23 (100-0)</b>	<b>9 (39-1)</b>
Ethiopia (N=8)	-	1 (12-5)	8 (100-0)	2 (25-0)
Egypt (N=4)	-	4 (100-0)	4 (100-0)	3 (75-0)
Nigeria (N=3)	1 (33-3)	2 (66-7)	3 (100-0)	2 (66-7)
Malawi (N=2)	-	-	2 (100-0)	-
Rwanda (N=2)	-	-	2 (100-0)	-
Kenya (N=1)	-	1 (100-0)	1 (100-0)	1 (100-0)
Sudan (N=1)	-	1 (100-0)	1 (100-0)	-
Tunisia (N=1)	-	1 (100-0)	1 (100-0)	1 (100-0)
Zimbabwe (N=1)	-	-	1 (100-0)	-

	Immunomodulators				
	Azathioprine	Cyclosporine	Mercaptopurine	Methotrexate	Tacrolimus
<b>Overall N=44*</b>					
<b>Asia N=21*</b>	<b>20 (95.2)</b>	<b>18 (85.7)</b>	<b>13 (61.9)</b>	<b>20 (95.2)</b>	<b>12 (57.1)</b>
India (N=9)*	9 (100.0)	8 (88.9)	7 (77.8)	9 (100.0)	7 (77.8)
Nepal (N=6)	1 (16.7)	6 (100.0)	4 (66.7)	6 (100.0)	3 (50.0)
Indonesia (N=2)	1 (50.0)	-	1 (50.0)	1 (50.0)	-
Pakistan (N=2)	2 (100.0)	2 (100.0)	-	2 (100.0)	1 (50.0)
Bangladesh (N=1)	1 (100.0)	1 (100.0)	-	1 (100.0)	-
Philippines (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)
<b>Africa N=23*</b>	<b>18 (78.3)</b>	<b>8 (34.8)</b>	<b>4 (17.4)</b>	<b>18 (78.3)</b>	<b>5 (21.7)</b>
Ethiopia (N=8)	7 (87.5)	2 (25.0)	-	5 (62.5)	-
Egypt (N=4)	4 (100.0)	1 (25)	-	4 (100.0)	-
Nigeria (N=3)	1 (50.0)	-	1 (33.3)	2 (66.7)	1 (33.3)
Malawi (N=2)	-	-	1 (50.0)	1 (50.0)	-
Rwanda (N=2)	2 (100.0)	2 (100.0)	-	2 (100.0)	2 (100.0)
Kenya (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)
Sudan (N=1)	1 (100.0)	1 (100.0)	-	1 (100.0)	1 (100.0)
Tunisia (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	-
Zimbabwe (N=1)	1 (100.0)	-	-	1 (100.0)	-
			<b>Surgeries</b>		
	<b>Ostomy</b>	<b>Small bowel resection</b>	<b>Colectomy</b>	<b>Strictureplasty</b>	<b>Ileoanal pouch</b>
<b>Overall N=44*</b>	<b>30 (68.2)</b>	<b>40 (90.9)</b>	<b>40 (90.9)</b>	<b>25 (56.8)</b>	<b>23 (52.3)</b>
<b>Asia N=21*</b>	<b>15 (71.4)</b>	<b>19 (90.5)</b>	<b>19 (90.5)</b>	<b>18 (85.7)</b>	<b>16 (76.2)</b>
India (N=9)*	8 (88.9)	8 (88.9)	8 (88.9)	9 (100.0)	8 (88.9)
Nepal (N=6)	5 (83.3)	6 (100.0)	6 (100.0)	5 (83.3)	5 (83.3)
Indonesia (N=2)	-	1 (50.0)	1 (50.0)	1 (50.0)	-
Pakistan (N=2)	1 (50.0)	2 (100.0)	2 (100.0)	1 (50.0)	1 (50.0)
Bangladesh (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)
Philippines (N=1)	-	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)
<b>Africa N=23*</b>	<b>15 (65.2)</b>	<b>21 (91.3)</b>	<b>21 (91.3)</b>	<b>7 (30.4)</b>	<b>7 (30.4)</b>
Ethiopia (N=8)	4 (50.0)	7 (87.5)	7 (87.5)	1 (12.5)	1 (12.5)
Egypt (N=4)	4 (100.0)	4 (100.0)	4 (100.0)	-	2 (50.0)
Nigeria (N=3)	2 (66.7)	3 (100.0)	3 (100.0)	2 (66.7)	2 (66.7)
Malawi (N=2)	2 (100.0)	2 (100.0)	2 (100.0)	1 (50.0)	1 (50.0)
Rwanda (N=2)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	-
Kenya (N=1)	-	1 (100.0)	1 (100.0)	-	-
Sudan (N=1)	-	-	-	-	-
Tunisia (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)
Zimbabwe (N=1)	-	1 (100.0)	1 (100.0)	-	-



	Biologic agents			
	Adalimumab	Adalimumab biosimilar	Infliximab	Infliximab biosimilar
<b>Overall N=44*</b>	<b>19 (43.2)</b>	<b>9 (20.5)</b>	<b>23 (52.3)</b>	<b>10 (22.7)</b>
<b>Asia N=21*</b>	<b>13 (61.9)</b>	<b>8 (38.1)</b>	<b>16 (76.2)</b>	<b>9 (42.9)</b>
India (N=9)*	8 (88.9)	8 (88.9)	8 (88.9)	8 (88.9)
Nepal (N=6)	2 (33.3)	6 (100.0)	4 (66.7)	-
Indonesia (N=2)	1 (50.0)	-	1 (50.0)	-
Pakistan (N=2)	1 (50.0)	-	1 (50.0)	-
Bangladesh (N=1)	-	-	1 (100.0)	-
Philippines (N=1)	1 (100.0)	-	1 (100.0)	1 (100.0)
<b>Africa N=23*</b>	<b>6 (26.1)</b>	<b>1 (4.3)</b>	<b>7 (30.4)</b>	<b>1 (4.3)</b>
Ethiopia (N=8)	-	-	-	-
Egypt (N=4)	4 (100.0)	-	4 (100.0)	-
Nigeria (N=3)	-	-	1 (33.3)	-
Malawi (N=2)	-	-	-	-
Rwanda (N=2)	-	-	-	-
Kenya (N=1)	1 (100.0)	-	1 (100.0)	-
Sudan (N=1)	-	-	-	-
Tunisia (N=1)	1 (100.0)	-	1 (100.0)	1 (100.0)
Zimbabwe (N=1)	-	1 (100.0)	-	-

\*One missing response from Sudan and one missing response from India excluded  
All values presented as mean (percent)

**Table 2.7.** Challenges faced by providers in LLMICs in managing Crohn's disease

	Management challenges							
	Lack of access to surgical management	Lack of access to biologics	TB reactivation on immunosuppressant	Patients unable to afford biologics	Patients unable to afford other treatments	Poor patient follow-up	Lack of psychosocial support for patients	Other
<b>Overall N=43*</b>	<b>7 (16.3)</b>	<b>21 (48.8)</b>	<b>11 (25.6)</b>	<b>28 (65.1)</b>	<b>18 (41.9)</b>	<b>18 (41.9)</b>	<b>14 (32.6)</b>	<b>1 (2.3)</b>
<b>Asia N=21*</b>	<b>2 (9.5)</b>	<b>6 (28.6)</b>	<b>7 (33.3)</b>	<b>12 (57.1)</b>	<b>7 (33.3)</b>	<b>6 (28.6)</b>	<b>5 (23.8)</b>	<b>1 (4.8)</b>
India (N=9)*	-	-	2 (22.2)	5 (55.6)	2 (22.2)	1 (11.1)	1 (11.1)	-
Nepal (N=6)	-	3 (50.0)	2 (33.3)	3 (50.0)	1 (16.7)	2 (33.3)	1 (16.7)	1 (16.7)
Indonesia (N=2)	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)	-
Pakistan (N=2)	-	1 (50.0)	-	1 (50.0)	1 (50.0)	-	-	-
Bangladesh (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	-
Philippines (N=1)	-	-	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	-
<b>Africa N=22*</b>	<b>5 (22.7)</b>	<b>15 (68.2)</b>	<b>13 (56.5)</b>	<b>16 (72.7)</b>	<b>13 (56.5)</b>	<b>12 (54.5)</b>	<b>9 (40.9)</b>	<b>-</b>
Ethiopia (N=8)	2 (25.0)	8 (100.0)	6 (75.0)	7 (87.5)	6 (75.0)	5 (62.5)	5 (62.5)	-
Egypt (N=4)	-	2 (50.0)	2 (50.0)	4 (100.0)	2 (50.0)	1 (25.0)	-	-
Nigeria (N=3)	-	2 (66.7)	2 (100.0)	2 (66.7)	2 (100.0)	2 (66.7)	2 (66.7)	-
Malawi (N=2)	1 (50.0)	1 (50.0)	-	1 (50.0)	-	1 (50.0)	1 (50.0)	-
Rwanda (N=2)	-	-	-	-	-	-	-	-
Kenya (N=1)	1 (100.0)	1 (100.0)	-	1 (100.0)	-	1 (100.0)	-	-
Tunisia (N=1)	-	-	1 (100.0)	-	1 (100.0)	1 (100.0)	1 (100.0)	-
Zimbabwe (N=1)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	-	-

\*Two missing responses from Sudan and one missing response from India excluded  
All values presented as mean (percent)

**Table 2.8.** Ranges of costs to patients of common Crohn's diagnostic tests overall, by region, and by country

	Colonoscopy with biopsy				
	<US \$50	US \$50-100	US \$100-500	>US \$500	Missing
<b>Overall N=44*</b>	<b>22 (50.0)</b>	<b>9 (20.5)</b>	<b>7 (15.9)</b>	<b>2 (4.5)</b>	<b>4 (9.1)</b>
<b>Asia N=21*</b>	<b>11 (52.4)</b>	<b>6 (28.6)</b>	-	<b>2 (9.5)</b>	<b>2 (9.5)</b>
India (N=9)*	5 (55.6)	4 (44.4)	-	-	-
Nepal (N=6)	5 (83.3)	1 (16.7)	-	-	-
Indonesia (N=2)	-	-	-	2 (100.0)	-
Pakistan (N=2)	-	1 (50.0)	-	-	1 (50.0)
Bangladesh (N=1)	-	-	-	-	1 (100.0)
Philippines (N=1)	1 (100.0)	-	-	-	-
<b>Africa N=23*</b>	<b>11 (47.8)</b>	<b>3 (13.0)</b>	<b>7 (30.4)</b>	-	<b>2 (8.7)</b>
Ethiopia (N=8)	6 (75.0)	-	2 (25.0)	-	-
Egypt (N=4)	3 (75.0)	1 (25.0)	-	-	-
Nigeria (N=3)	-	-	2 (66.7)	-	1 (33.3)
Malawi (N=2)	1 (50.0)	-	-	-	-
Rwanda (N=2)	-	2 (100.0)	-	-	-
Kenya (N=1)	-	-	1 (100.0)	-	-
Sudan (N=1)	1 (100.0)	-	-	-	-
Tunisia (N=1)	-	-	1 (100.0)	-	-
Zimbabwe (N=1)	-	-	1 (100.0)	-	-
	Upper endoscopy with biopsy				
	<US \$50	US \$50-100	US \$100-500	>US \$500	Missing
<b>Overall N=44*</b>	<b>31 (70.5)</b>	<b>7 (15.9)</b>	<b>6 (13.6)</b>	-	-
<b>Asia N=21*</b>	<b>17 (81.0)</b>	<b>2 (9.5)</b>	<b>2 (9.5)</b>	-	-
India (N=9)*	5 (55.6)	4 (44.4)	-	-	-
Nepal (N=6)	8 (88.9)	1 (11.1)	-	-	-
Indonesia (N=2)	-	-	2 (100.0)	-	-
Pakistan (N=2)	1 (50.0)	1 (50.0)	-	-	-
Bangladesh (N=1)	1 (100.0)	-	-	-	-
Philippines (N=1)	1 (100.0)	-	-	-	-
<b>Africa N=23*</b>	<b>14 (60.9)</b>	<b>5 (21.7)</b>	<b>4 (17.4)</b>	-	-
Ethiopia (N=8)	5 (62.5)	2 (25.0)	1 (12.5)	-	-
Egypt (N=4)	4 (100.0)	-	-	-	-
Nigeria (N=3)	2 (66.7)	-	1 (33.3)	-	-
Malawi (N=2)	2 (100.0)	-	-	-	-
Rwanda (N=2)	-	2 (100.0)	-	-	-
Kenya (N=1)	-	-	1 (100.0)	-	-
Sudan (N=1)	1 (100.0)	-	-	-	-
Tunisia (N=1)	-	1 (100.0)	-	-	-
Zimbabwe (N=1)	-	-	1 (100.0)	-	-

	Abdominal CT scan				
	<US \$50	US \$50-100	US \$100-500	>US \$500	Missing
<b>Overall N=44*</b>	<b>9 (20.5)</b>	<b>16 (36.4)</b>	<b>12 (27.3)</b>	<b>1 (2.3)</b>	<b>6 (13.6)</b>
<b>Asia N=21*</b>	<b>3 (14.3)</b>	<b>8 (38.1)</b>	<b>5 (23.8)</b>	-	<b>5 (23.8)</b>
India (N=9)*	-	3 (33.3)	3 (33.3)	-	3 (33.3)
Nepal (N=6)	1 (16.7)	2 (33.3)	1 (16.7)	-	2 (33.3)
Indonesia (N=2)	-	2 (100.0)	-	-	-
Pakistan (N=2)	2 (100.0)	-	-	-	-
Bangladesh (N=1)	-	-	1 (100.0)	-	-
Philippines (N=1)	-	1 (100.0)	-	-	-
<b>Africa N=23*</b>	<b>6 (26.1)</b>	<b>8 (34.8)</b>	<b>7 (30.4)</b>	<b>1 (4.3)</b>	<b>1 (4.3)</b>
Ethiopia (N=8)	1 (12.5)	7 (87.5)	-	-	-
Egypt (N=4)	3 (75.0)	1 (25.0)	-	-	-
Nigeria (N=3)	2 (66.7)	-	1 (33.3)	-	-
Malawi (N=2)	-	-	1 (50.0)	1 (50.0)	-
Rwanda (N=2)	-	-	2 (100.0)	-	-
Kenya (N=1)	-	-	1 (100.0)	-	-
Sudan (N=1)	-	-	-	-	1 (100.0)
Tunisia (N=1)	-	-	1 (100.0)	-	-
Zimbabwe (N=1)	-	-	1 (100.0)	-	-
	Stool culture				
	<US \$50	US \$50-100	US \$100-500	>US \$500	Missing
<b>Overall N=44*</b>	<b>28 (63.6)</b>	<b>3 (6.8)</b>	<b>3 (6.8)</b>	-	<b>10 (22.7)</b>
<b>Asia N=21*</b>	<b>9 (42.9)</b>	<b>2 (9.5)</b>	<b>2 (9.5)</b>	-	<b>8 (38.1)</b>
India (N=9)*	3 (33.3)	1 (11.1)	-	-	5 (55.6)
Nepal (N=6)	3 (50.0)	1 (11.1)	-	-	3 (50.0)
Indonesia (N=2)	-	-	2 (100.0)	-	-
Pakistan (N=2)	1 (50.0)	1 (50.0)	-	-	-
Bangladesh (N=1)	1 (100.0)	-	-	-	-
Philippines (N=1)	1 (100.0)	-	-	-	-
<b>Africa N=23*</b>	<b>19 (82.6)</b>	<b>1 (4.3)</b>	<b>1 (4.3)</b>	-	<b>2 (8.7)</b>
Ethiopia (N=8)	8 (100.0)	-	-	-	-
Egypt (N=4)	3 (75.0)	1 (25.0)	-	-	-
Nigeria (N=3)	3 (100.0)	-	-	-	-
Malawi (N=2)	1 (50.0)	-	-	-	1 (50.0)
Rwanda (N=2)	2 (100.0)	-	-	-	-
Kenya (N=1)	-	-	1 (100.0)	-	-
Sudan (N=1)	-	-	-	-	1 (100.0)
Tunisia (N=1)	1 (100.0)	-	-	-	-
Zimbabwe (N=1)	1 (100.0)	-	-	-	-

\*One missing response from Sudan and one missing response from India excluded  
All values presented as mean (percent)

**Table 2.9.** Ranges of costs to patients of common Crohn's disease treatments

	<b>Hospitalization for Crohn's flare</b>						
	<b>&lt;\$100</b>	<b>\$101-500</b>	<b>\$501-1000</b>	<b>\$1001-2000</b>	<b>2001-5000</b>	<b>&gt;\$5000</b>	<b>Missing</b>
<b>Overall N=44*</b>	<b>5 (11.6)</b>	<b>17 (39.5)</b>	<b>4 (9.3)</b>	<b>5 (11.6)</b>	<b>1 (2.3)</b>	<b>1 (2.3)</b>	<b>10 (23.3)</b>
<b>Asia N=21*</b>	<b>1 (4.8)</b>	<b>8 (38.1)</b>	<b>2 (9.5)</b>	<b>1 (4.8)</b>	-	<b>1 (4.8)</b>	<b>8 (38.1)</b>
India (N=9)*	-	3 (33.3)	1 (11.1)	1 (11.1)	-	-	4 (44.4)
Nepal (N=6)	1 (16.7)	1 (16.7)	-	-	-	-	4 (66.7)
Indonesia (N=2)	-	2 (100.0)	-	-	-	-	-
Pakistan (N=2)	-	1 (50.0)	-	-	-	1 (50.0)	-
Bangladesh (N=1)	-	-	1 (100.0)	-	-	-	-
Philippines (N=1)	-	1 (100.0)	-	-	-	-	-
<b>Africa N=23*</b>	<b>4 (18.2)</b>	<b>9 (40.9)</b>	<b>2 (9.1)</b>	<b>4 (18.2)</b>	<b>1 (4.5)</b>	-	<b>2 (9.1)</b>
Ethiopia (N=8)	3 (37.5)	4 (50.0)	1 (12.5)	-	-	-	-
Egypt (N=4)	-	3 (75.0)	-	1 (12.5)	-	-	-
Malawi (N=2)	1 (50.0)	-	-	-	-	-	1 (50.0)
Nigeria (N=3)	-	1 (33.3)	1 (33.3)	1 (33.3)	-	-	-
Rwanda (N=2)	-	-	-	1 (50.0)	-	-	1 (50.0)
Kenya (N=1)	-	-	-	-	1 (100.0)	-	-
Tunisia (N=1)	-	1 (100.0)	-	-	-	-	-
Zimbabwe (N=1)	-	-	-	1 (100.0)	-	-	-
	<b>Biologic agents</b>						
	<b>&lt;\$50</b>	<b>\$50-100</b>	<b>\$100-500</b>		<b>&gt;\$500</b>	<b>Missing</b>	
<b>Overall N=44*</b>	<b>2 (4.7)</b>	<b>4 (9.3)</b>	<b>12 (27.9)</b>		<b>14 (32.6)</b>	<b>11 (25.6)</b>	
<b>Asia N=21*</b>	<b>1 (4.8)</b>	<b>2 (9.5)</b>	<b>4 (19.0)</b>		<b>8 (38.1)</b>	<b>6 (28.6)</b>	
India (N=9)*	1 (11.1)	-	2 (22.2)		3 (33.3)	3 (33.3)	
Nepal (N=6)	-	1 (16.7)	2 (33.3)		1 (16.7)	2 (33.3)	
Indonesia (N=2)	-	-	-		2 (100.0)	-	
Pakistan (N=2)	-	-	-		1 (50.0)	1 (50.0)	
Bangladesh (N=1)	-	-	-		1 (100.0)	-	
Philippines (N=1)	-	1 (100.0)	-		-	-	
<b>Africa N=23*</b>	<b>1 (4.5)</b>	<b>2 (9.1)</b>	<b>8 (36.4)</b>		<b>6 (27.3)</b>	<b>5 (22.7)</b>	
Ethiopia (N=8)	1 (12.5)	-	2 (25.0)		4 (50.0)	1 (12.5)	
Egypt (N=4)	-	2 (50.0)	1 (25.0)		1 (25.0)	-	
Malawi (N=2)	-	-	-		-	2 (100.0)	
Nigeria (N=3)	-	-	2 (66.7)		1 (33.3)	-	
Rwanda (N=2)	-	-	-		-	2 (100.0)	
Kenya (N=1)	-	-	1 (100.0)		-	-	
Tunisia (N=1)	-	-	1 (100.0)		-	-	
Zimbabwe (N=1)	-	-	1 (100.0)		-	-	

\*Two missing responses from Sudan and one missing response from India excluded  
All values presented as mean (percent)

## Site visit summaries

### Asian Institute of Gastroenterology, Hyderabad March 25-26, 2019

Asian Institute of Gastroenterology (AIG) is a large super specialty referral hospital in Hyderabad, India. AIG started small, and through private donations has quickly grown into the largest gastroenterology hospital in the world, opening their expansive and advanced hospital early last year. Although AIG is a private institution, its underlying ideology is providing the highest possible GI care at the lowest cost to the patient. It is led by Chairman Dr. Nageshwar Reddy, former president of the World Endoscopy Organization, winner of the most prestigious gastroenterology and endoscopy awards, and pioneer in GI endoscopy, particularly in therapeutic pancreaticobiliary endoscopy and innovations in transgastric endoscopic surgery. Dr. Rupa Banerjee is the director of the IBD clinic at AIG and has recently initiated the IBD – Emerging Economies (IBD-EE) group with 16 countries in South Asia and the Middle East. Patients travel from all over Asia and the world to be seen by Dr. Reddy and Dr. Banerjee.

The 30 gastroenterologists at AIG perform at least 300 upper endoscopies and 100 colonoscopies each day in 29 state of the art endoscopy procedure rooms. Dr. Banerjee has an impressive cohort of over 4,000 IBD patients that she actively collects and stores data on in an electronic database. She reported that she has noticed an overall increasing trend in IBD in India, with more Crohn's disease in



Top: PI Ruma Rajbhandari (left) and project manager Samantha Smith (right) with Dr. Rupa Banerjee at AIG's IBD clinic. Middle: Dr. Nageshwar Reddy performing endoscopy in AIG's mobile clinic. Bottom: Mobile vans that transmit data back to AIG. Middle and bottom photos adapted from Talukdar & Reddy, Making endoscopy mobile: The journey. *Digestive Endoscopy* (2012).



South India, and more UC in North India. Patients usually come to Dr. Banerjee after many years of symptoms and misdiagnosis from local clinics and district hospitals, who may not have access to any form of endoscopy. Patients have usually been treated with anti-TB therapy and other antibiotics with little relief. She diagnoses IBD based on clinical symptoms, colonoscopic findings, and tissue pathology.

One major challenge gastroenterologists at AIG face in diagnosing Crohn's disease is differentiating between Crohn's and intestinal TB, which symptomatically and endoscopically overlaps with Crohn's. Dr. Banerjee uses TB-PCR to test for active TB in patients she suspects Crohn's but noted a 5-10% false negative rate. If a patient is determined not to have active TB, her first-choice medication for treating Crohn's is Azathioprine, an

immunosuppressant that is widely used to treat IBD in India and Nepal. If a patient does not respond to Azathioprine, Dr. Banerjee would next consider biologics, but then faces her second challenge of the incredibly high cost of biologics in India. A single dose of Infliximab costs \$1700 USD, which is almost equal to yearly income per capita in India, making it unaffordable to almost everyone who needs it. Most patients in India pay out of pocket for their medical expenses, although AIG does what they can to assist their poorest patients who cannot afford their care.

A priority for Dr. Reddy and Dr. Banerjee is reaching the nearly 70% of the Indian population that lives in rural villages and the one-third of Indians who live below the poverty line, who do not have access to advanced health facilities and doctors. In 2006, they started the Rural Health Care Project, with the goal of improving rural health

by providing free diagnostic and clinical services to the poor rural populations of the 23 districts and 30,000 villages in the state of Andhra Pradesh. The program consists of three mobile busses customized with a modern upper endoscopy and colonoscopy unit, transabdominal ultrasonography, and basic laboratory, that travel to the rural villages and provide free diagnostics and medications. The team of physicians and technicians spends three days in each village, during which they screen local villagers at base camps for problems requiring further work-up, provide medical consultations to screened patients, perform any necessary diagnostic procedures, and offer free medicines to those with a diagnosis. Epidemiologic data is also collected on the approximately 20 million patients that Dr. Reddy estimates have been reached. He said his ultimate goal is to reach all 80 million people across Andhra Pradesh. ■

## **Raipur Medical College Hospital, Raipur, Chhattisgarh March 27, 2019**



**Endoscopy suite at Raipur Medical College.**

This is the main teaching hospital associated with Raipur Medical College. We met with three doctors (Dr. Sandeep Chandrakar, Dr. Rajendra Ratre and Dr. Amit Agrawal) who were all surgeons carrying out endoscopy at the hospital as there was not a medical gastroenterologist at the hospital. The hospital is a public institution with many patients getting free care through a special card that identifies them as falling below the poverty line, through the National Health Insurance Scheme. Even when there are costs for procedures, they are quite minimal. For example, a Whipple operation costs Rs. 500. The endoscopy suite at the hospital is a single room with several Pentax endoscopy tower systems, not

all of which were being used. They had one functional and one non-functional upper endoscope, one functional colonoscope, one rigid sigmoidoscope, which was out of order, and one ERCP scope which they had not yet used. They rarely gave anesthesia for upper endoscopies and colonoscopies. There were many (6-10) providers at the hospital who could perform upper endoscopies but fewer (3) who could perform colonoscopies. Most of the procedures they carried out were diagnostic, rather than therapeutic—for example, they did not do variceal banding. They did keep an endoscopy registry but only had a few years of data due to limitations of computer hard drive space. ■



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## **DKS Postgraduate Institute and Research Center, Raipur, Chhattisgarh March 27, 2019**

This is a new, public, super-specialty hospital in Raipur with approximately 400 general beds and 50 ICU beds. Its website mentions the availability of flow cytometry, chromatography (HPLC, FPLC), molecular biology, positron emission tomography (PET) and

genetic studies. A BSL-III laboratory for mycobacteria is under construction. It appears to focus on Neurosurgery, Pediatric Surgery, Plastic Surgery and Cardiology. We met with Dr. Anish Goenka who is a surgeon performing endoscopy at the hospital. The hospital

had only recently opened and thus he was still getting gastroenterology services off the ground. He stated that he had done about 10 upper endoscopies and 2 colonoscopies in the last 3 months. The hospital had advanced diagnostic services.

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## **MMI Narayana Multispeciality Hospital, Raipur, Chhattisgarh March 27, 2019**

This is a 250-bed private tertiary hospital managed by Narayana Health--a brand strongly associated with a mission to deliver high-quality, affordable healthcare services to the broader population by leveraging economies of scale, skilled doctors, and an efficient business model.

We met with Dr. Abhishek Jain, one of two gastroenterologists based at the hospital. Overall, this facility was well equipped with a GI surgeon as well as two medical gastroenterologists. They had two upper endoscopes, one colonoscope, one ERCP scope and one EUS

scope. The only gastroenterology procedures not available were double balloon enteroscopy and video capsule endoscopy. There was one procedure room with most procedures being done without anesthesia in that room. Any procedures requiring anesthesia were done in the operating room. ■

## Ram Krishna Care, Raipur, Chhattisgarh March 28-29, 2019



Left: Endoscopy suite at Ram Krishna Care. Right: Automated endoscope reprocessor at Ram Krishna Care.

This is a 400-bed private, tertiary care hospital in Raipur. We met with Dr. Sandeep Pandey at the hospital, one of five providers carrying out endoscopies at the hospital. The GI department at the hospital was well equipped, carrying out everything from basic upper endoscopies and colonoscopies to single balloon enteroscopy. There were two procedure rooms and a separate scope cleaning/reprocessing area (Appendix Figure 3.1.6). They were one of the few facilities with an automatic scope washer. They had four upper endoscopes, three colonoscopes, two ERCP scope, one EUS scope and one enteroscope. ■



## All India Institute of Medical Sciences, New Delhi March 28-29, 2019

AIIMS is a large public tertiary research and teaching hospital located in Delhi with a very busy IBD clinic run by two IBD specialists Dr. Vineet Ahuja and Dr. Saurabh Kedia. Being a public institution, AIIMS' facilities were not quite as advanced as at AIG, but most services including endoscopy and colonoscopy are provided free of charge for most patients. The endoscopy suite consists of two rooms, one with

three beds for endoscopies and colonoscopies, and one ERCP room, in which AIIMS doctors and fellows perform approximately 70 upper endoscopies and 10-15 colonoscopies per day. Upper endoscopies and colonoscopies are all performed without sedation, unless required by the patient, which dramatically increases the speed with which they are able to complete procedures. The speed of procedures and immense

patient volume also means that there is not time to use automatic endoscope reprocessors, and so all scopes are cleaned manually so they can quickly be reused.

Dr. Ahuja maintains an IBD database of over 5,000 patients, approximately 1,000 of which are diagnosed with Crohn's disease. He estimates that approximately 70% of the IBD patients he sees at AIIMS are poor.



As at AIG, Dr. Ahuja and Dr. Kedia expressed that their most significant challenge is in distinguishing a Crohn's disease diagnosis from intestinal TB. Their typical approach is to empirically treat patients for TB first and consider Crohn's disease only if they don't respond. In the last few years, Dr. Ahuja and Dr. Kedia have focused much of their research on this topic, publishing numerous studies on the accuracy of certain imaging features and biomarkers that may help in the discernment of Crohn's from TB. Their ultimate goal is to create an algorithm for gastroenterologists in their part of the world to use to more quickly and accurately diagnose and treat Crohn's disease and intestinal TB. In addition to running the IBD clinic at AIIMS, Dr. Ahuja is also the associate dean of research and assists in overseeing the cutting-edge biorepository and research facility. Dr. Ahuja is also conducting an IBD incidence/prevalence study in the more rural area of Kolkata, where they have partnered with a Public Health institute to provide diagnostic testing to symptomatic patients. They are surveying people door to door for GI symptoms, carrying out fecal occult blood testing and if positive, fecal calprotectin. If this is positive, they get a more advanced work up, including colonoscopies. Researchers are currently collecting data on this study. ■

**Top: Manual endoscope cleaning between patients at AIIMS. Bottom: Automated endoscope reprocessors at AIIMS that were not used due to high patient volume.**



## Institute of Medicine/T.U. Teaching Hospital, Kathmandu March 31, 2019

T.U. Teaching Hospital is a large public tertiary teaching hospital run by the Institute of Medicine in Kathmandu. We met Dr. Rahul Pathak, a faculty member and attending gastroenterologist at Institute of Medicine (IOM). The gastroenterologists at IOM do approximately 40 upper endoscopies and 10-15 colonoscopies per day, despite only having two functioning endoscopes and two colonoscopes, and a shortage of other instruments necessary for performing endoscopy and diagnosing IBD. The endoscopy nurses clean the scopes manually

between patients, and also clean disposable instruments such as biopsy forceps to reuse until they break.

Dr. Pathak told us that he has noted a recent increase in IBD patients in the last two years, mainly from the Terai region of Nepal, as well as in Nepalis who have recently traveled to the Middle East and other parts of the world. They see approximately three UC patients every week at IOM but have only had one Crohn's disease patient in the last three months. He estimated 95% of IBD patients in Nepal have UC, and 5% have Crohn's.

IBD patients at IOM have often had symptoms for years and have been treated numerous times for infection or hemorrhoids before having any endoscopy or colonoscopy. Dr. Pathak also indicated differentiation between Crohn's and TB as the primary diagnostic challenge, which they attempt to accomplish through histopathology and chest CT, but usually need to treat with anti-TB therapy before considering Crohn's. The cost and unavailability of biologics and Nepal is also a barrier, and most IBD patients are treated with Mesalamine or Azathioprine. ■



Endoscopy facility at Institute of Medicine T.U. Teaching Hospital.

## Bir Hospital, Kathmandu March 31, 2019

ITEMS	RATE
1 GASTROSCOPY	750
2 COLONOSCOPY	2000
3 ERCP DIAGNOSTIC	4000
4 ERCP THERAPEUTIC	7000
5 > SPHINCTEROTOMY	7000
6 > STENTING	7000
7 > STONE EXTRCTION	7000
8 > PANCREATIC DUCT STENTING	7000
9 POLYPECTOMY	4000
10 ESOPHAGEAL DIALATATION	3000
11 SCLEROTHERAPY	3000
12 BANDING OF ESOPHAGEAL VARICES	4000
13 GASTRIC VARICEAL GLUE INT.	6000
14 F.B. REMOVAL	5000

Bir Hospital is another public tertiary hospital in Kathmandu. We met with Dr. Bhupendra Basnet, the director of the gastroenterology department, as well as several other gastroenterologists and fellows. They have a busy endoscopy suite, performing 120-150 upper endoscopies and 30-40 colonoscopies every week. Dr. Basnet estimated they have seen approximately 1-2 Crohn's patients and 4-5 UC patients at Bir Hospital in the last six months. He explained that IBD patients have usually had symptoms for many years and have been misdiagnosed due to the lack of endoscopy and colonoscopy services at district hospitals. This is a major barrier to rural IBD patients, who have a difficult time coming to Kathmandu for regular follow-up appointments. The doctors also noted that most of the patients who come to Bir Hospital are poor, and that the majority of Crohn's patients in Nepal seek care at private facilities. ■

**Cost of endoscopy procedures at Bir Hospital, hanging in the endoscopy suite waiting area.**

## Dhulikhel Hospital, Dhulikhel April 1, 2019

Dhulikhel Hospital is a non-profit community-based hospital, located about 30 km outside of Kathmandu in the semi-rural area of Dhulikhel. This was by far the most advanced endoscopy facility we visited in Nepal, largely due to the significant support they receive from a German NGO. We met Dr. Ram Gurung, chief interventional endoscopist at Dhulikhel Hospital. The gastroenterologists at Dhulikhel Hospital perform 10 upper endoscopies and 1-2 colonoscopies per day but see very little IBD. In the ten years Dr. Gurung has practiced at Dhulikhel Hospital he reported

they have had approximately 20 UC cases and only four Crohn's cases. He said that most IBD patients he has seen are between 20 and 35 years old, and described them as lower-middle class. He also reported the overlap with more prevalent intestinal TB, as well as the cost and lack of availability of biologics in Nepal are the main barriers in the diagnosis and management of Crohn's and IBD patients. The endoscopy unit at Dhulikhel was by far the most advanced we saw on our trip, with all of the highest tech equipment and spacious procedure rooms. Dhulikhel Hospital endoscopy suite is a prime

example of how external support can improve quality of gastroenterology services in Nepal. ■



Top: Three bucket manual scope cleaning. Bottom: ERCP room at Dhulikhel Hospital.

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## **Nidan Hospital, Patan** **April 3, 2019**

Dr. Neeraj Joshi, a gastroenterologist at the private Nidan Hospital, is considered to be Nepal's IBD expert. Most cases of confirmed or suspected IBD in Nepal are referred to Dr. Joshi by other providers.

Dr. Joshi has started maintaining his own IBD database in the last two years, and according to records has seen approximately 120-130 IBD patients in that time. He estimates approximately 40 of these patients are diagnosed with Crohn's. Despite the hospital being private, Dr. Joshi

reported that most of his patients are middle class, as Nepal's wealthiest patients usually choose to seek care outside of the country in India. Availability and cost of biologics is a challenge for Nidan Hospital's IBD patients as well, and Dr. Joshi primarily uses corticosteroids and immunomodulators to manage Crohn's. He mentioned that he can think of at least five of his patients who need biologic therapy but cannot afford it. Dr. Joshi feels that what he is seeing as far as IBD in Nepal is just

the tip of the iceberg, and there are likely many undiagnosed, particularly the elderly and those in rural areas who cannot access specialized care. When asked how he would treat all Crohn's disease patients in Nepal, he said he would start by ensuring basic IBD care where the patient lives by training as many doctors as possible in IBD diagnosis and management through case discussions, which would improve their ability to identify very sick patients and refer them for advanced diagnostics or surgery. ■

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## **Patan Hospital, Patan** **April 4, 2019**

Our last stop was a brief visit to Patan Hospital, a public tertiary hospital just outside of Kathmandu, where we met with gastroenterologist Dr. Yuba Raj Sharma. Patan Hospital is in the process of building a new gastroenterology unit and recently purchased the equipment to perform

ERCP and EUS. Dr. Sharma estimated that only 5% of their IBD patients are diagnosed with Crohn's disease and also identified diagnostic overlap with TB and cost of biologics as the most pressing challenges. He said they always consider TB first because it is so much more prevalent, often

treating patients with a full 6 months of anti-TB therapy before thinking of Crohn's. Dr. Sharma mentioned attempting to start an IBD society in Nepal in the past, and is enthusiastic about participating in a country-wide and a multi-country registry of IBD patients. ■

# Pakistan

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## **Sindh Institute of Urology and Transplantation, Karachi** **July 23, 2019**

This hospital is a dialysis and kidney transplant center and public teaching hospital located in Sukkur, Karachi. It was founded in 1970 and remains Pakistan's largest kidney disease center and largest public sector health organization. In 2003, doctors and surgeons at SIUT conducted the country's very first liver transplant. Medical treatment is provided for free, which is why most patients are predominantly from rural and poorer urban strata with little to no access to medical facilities and care. Regarding

funding, SIUT has a collaborative model between the government and the community: donations from the public, from corporate organizations, government grants, and religious charity make up the funding. SIUT also professionally trains doctors, nurses, and technicians in-house.

Dr. Abbas Ali Tasneem of SIUT has about 5-10 years of experience with managing inflammatory bowel disease and is among the several other providers in the Gastroenterology

department who perform endoscopies and colonoscopies. He has noted that ulcerative colitis is the most common form of IBD, and he mentioned that biologics are too expensive to obtain because of a higher demand for them. Surgical complications such as strictures and fistulas are rare, and when they do occur, the surgeon on staff is consulted. Dr. Tasneem also noted that there have not been any deadly Crohn's disease cases that he has come across yet. ■

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## **Dow University Hospital, National Institute of Liver and GI Diseases, Karachi** **July 24, 2019**

This 800-bed hospital was established in 2009 and serves patients with modern facilities and treatment for both complex and routine medical problems. Included in the hospital are endoscopy units, a nursery, ICU, HDU, and more. The hospital is supported with the diagnostic facilities from Dow Diagnostic & Research laboratories and Dow Radiology. While services

are not free for patients, costs for care are known to be relatively affordable and of high quality. The hospital also provides training for undergraduate and postgraduate medical students. Dr. Muhammad Majeed, a gastroenterologist and consultant, discussed his experience treating IBD in the hospital. He talked about the access and availability to endoscopy and colonoscopy

services within the facility, as well as radiology and pathology services. Although he has only seen 1-2 Crohn's disease patients in the past year, he is confident in Dow's treatment availabilities in handling the disease. While the hospital does not have access to biologic agents (with the exception of Infliximab), they do have all other treatments and medications needed to address IBD. ■

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## **The Indus Hospital, Karachi** **July 24, 2019**

Indus Hospital was founded in the hopes of alleviating the health issues of poverty-stricken patients in Karachi. It developed into a multi-disciplinary tertiary care hospital that serves the underserved population of Pakistan with free and high-quality treatment. It is a 150-bed hospital that operates solely on public donations and government grants. They have a strong

and thriving research center which we communicated with before interviewing one of their lead gastroenterology consultants, Dr. Manzoor Hussain. Dr. Hussain noted that of the 15 IBD patients seen in the past year, only one of them had Crohn's disease. Yet, he reported that the hospital had all the necessary diagnostic and lab facilities in order to assess Crohn's and treat

it (with the exception of biologics). Indus Hospital performs hundreds of endoscopies and colonoscopies every year, and has experience taking biopsies. The gastroenterologists also work with formally trained pathologists regularly. He also noted that Ulcerative Colitis is increasing in his patient population, but Crohn's is still too rare to notice any trends. ■

**Appendix 3.4.** Summary of Asia site visits

Facility name	Facility type	Location	Providers	# IBD	# CD	# Upper endos/day	# Colons /day	Challenges	Opportunities
<b>Asian Institute of Gastroenterology</b>	Private	Hyderabad, India	<b>Dr. Rupa Banerjee</b> <b>Dr. Nageshwar Reddy</b>	4,000-5,000	~1,000	300	100	- Cost of biologics - Differentiation between CD and TB- TB reactivation on immunosuppressant therapy	- New AIG: large super specialty referral hospital (largest GI hospital in the world) - large IBD cohort - Mobile endoscopy vans - Opportunity to develop public sector gastroenterologists
<b>Raipur Medical College</b>	Public	Raipur, India	<b>Dr. Sandeep Chandrakar</b> <b>Dr. Rajendra Ratre</b> <b>Dr. Amit Agrawal</b>	4-5 in past 10 years	0-1	2-3	1-2	- No gastroenterologists in the public sector	- Opportunity to develop public sector gastroenterologists
<b>Ram Krishna Care</b>	Private	Raipur, India	<b>Dr. Sandeep Pandey</b>	~250	60-70	12-15	5-8	- Differentiation between CD and TB- Cost of diagnostics and treatments	
<b>DKS PG Institute</b>	Public	Raipur, India	<b>Dr. Ashisk Goenka</b>	1-2 in past 3 years	0	<1 (40/year)	<1 (8/year)		
<b>MMI Narayana</b>	Private	Raipur, India	<b>Dr. Abishek Jain</b>	20 in 1 year	8	8	<1 (8/month)	- Cost of diagnostics and treatments - Patient follow-up is a problem	
<b>All India Institute of Medical Sciences</b>	Public	Delhi, India	<b>Dr. Vineet Ahuja</b> <b>Dr. Saurabh Kedia</b>	5,840	~1,000	70	10-15	- Cost of biologics - TB reactivation on immunosuppressants	- Large cohort of Crohn's patients - Committed academics - Kolkata-based IBD study
<b>Institute of Medicine/ Teaching Hospital</b>	Public	Kathmandu, Nepal	<b>Dr. Rahul Pathak</b>	~15 per month	1-2 per month	40	10-15	- Differentiation between CD and TB- Lack of reliable pathologists, one gastro pathologist in Nepal (private)	- Recently started IBD data collection
<b>Dhulikhel Hospita</b>	Community hospital, lots of external support	Dhulikhel, Nepal	<b>Dr. Ram Gurung</b>	24 in >10 years	4	10	1-2	- Differentiation between CD and TB- Cost of diagnostics and treatments - Unavailability of biologics in Nepal	- Model of high quality foreign-funded endoscopy suite - Potential for research
<b>Nidan Hospital</b>	Private	Patan, Nepal	<b>Dr. Neeraj Joshi</b>	120-130	40	12-15	5-8	- Cost and unavailability of biologics	- Known as Nepal's IBD expert
<b>Patan Hospital</b>	Public	Patan, Nepal	<b>Dr. Yuba Raj Sharma</b>	~500	25	8-10	2-4	- Cost and unavailability of biologics - Differentiation between CD and TB	

<b>Sindh Institute of Urology and Transplant (SIUT)</b>	Public	Karachi, Pakistan	<b>Dr. Abbas Ali Tasneem</b>	50-70 per year	5% – 10% of IBD cases	1,500 in past 6 months	500 in past 6 months	-Lack of efficient and available biologics -Patient advocacy is not strong -Differentiation between CD and TB	
<b>The Indus Hospital</b>	Privately run but funded by philanthropic donations	Karachi, Pakistan	<b>Dr. Manzoor Hussain</b>	20-30 per year	1	1,900 in past 6 months		-Lack of sufficient funds to keep up with treatment -Lack of response to certain treatments makes the provider resort to more expensive treatment	-Large amounts of donations to the hospital in the past year
<b>Dow University Hospital</b>	Public	Karachi, Pakistan	<b>Dr. Muhammad Majeed</b>	15-20	1-2	600 in past 6 months	300-400 in past 6 months	-Alternative medicine can interfere with treatment -Patients come too late - Differentiation between CD and TB	





# Malawi

## Queen Elizabeth Central Hospital (QECH), Blantyre August 19, 2019

Queens Hospital in Blantyre is one of four public academic hospitals affiliated with the University of Malawi College of Medicine and is located in the large city of Blantyre. Queens is home to Malawi's only medically trained gastroenterologist, a former UK NHS physician, Dr. Peter Finch, as well as Malawi's WGO endoscopy training center. Although Dr. Finch is the only provider at Queens who does colonoscopy, he has helped train several other surgeons and internists in upper endoscopy, including dilation of esophageal strictures. The endoscopy suite at Queens consists of a combined waiting and recovery area and one large procedure room. Both upper endoscopy (200+ per month) and colonoscopy (11-50 per

month) are done regularly at Queens, as well as bougie dilation, but they do not have advanced procedures such as ERCP or capsule endoscopy. While the endoscopy suite was stocked with basic instruments such as forceps and injection needles, they sometimes have to get creative by making bands out of pediatric urinary catheters.

In the last five years that he has been there, Dr. Finch reports having seen one proven case of Crohn's disease, in a young boy, and a handful of suspected UC cases. This patient was not diagnosed until his fourth hospital admission after a six-year period of diagnostic delay. He presented with severe slow-growing skin ulcers, for which he was previously treated

with anti-TB therapy, IV antibiotics, and skin grafting. Colonoscopy with biopsy was suggestive of Crohn's disease, leading to a diagnosis of pyoderma gangrenosum associated with Crohn's. He was treated with prednisone and Azathioprine and improved rapidly. Dr. Finch emphasized the challenges he faces in diagnosing GI diseases due to patient's inability to afford the exorbitant cost patients must pay out of pocket for histology. This is a major barrier to accurately diagnosing Crohn's due to the crucial role of taking biopsies and analyzing tissue pathology. This, combined with lack of access to a trained gastroenterologist for much of the country, likely leads to quite a bit misdiagnosis of IBD. ■



**Left: Queens endoscopy suite instrument cabinet. Right: Providers preparing a patient for endoscopy at Queens Hospital.**

# Malawi

## Neno District Hospital, Neno August 20, 2019

Neno District Hospital is a PIH-supported district hospital in rural Malawi, a 2-3-hour drive outside of Blantyre. Although the district hospital did not have endoscopy or any gastroenterologists, the providers at Neno District Hospital frequently refer patients to Queens for endoscopy but often face challenges in having them scheduled in a timely manner. In fact, during our visit, there was a patient with likely upper gastrointestinal bleeding, receiving blood transfusions who was being referred to Queens for upper endoscopy but the Neno doctors expressed concern that he might not get the upper endoscopy for several weeks due to the long wait list at Queens.

Despite their inability to diagnose Crohn's disease, Neno District Hospital has an impressive integrated chronic care clinic modeled after

the successful HIV platform of care, applying it to NCDs such as hypertension and diabetes. ■



**Top: Neno District Hospital. Bottom: Patient reception, triage, and waiting area for the integrated chronic care clinic at Neno District Hospital.**

# Ethiopia

## Black Lion Hospital, Addis Ababa August 22, 2019

Black Lion Hospital is a large tertiary hospital in Ethiopia's capital city of Addis Ababa that is both government and privately funded. Black Lion has nine gastroenterologists, all of whom perform upper endoscopy and colonoscopy. It is also the only hospital of the six we visited in Africa that performed advanced endoscopic procedures such as ERCP and EUS. The endoscopy suite had three procedure rooms, a separate scope cleaning/reprocessing room where scopes are manually cleaned using the three-bucket system, and a large storage closet with a scope drying cabinet and plenty of scopes.

Both Dr. Yohannes Birhanu and Dr. Rezene Behre reported that the number of Crohn's disease patients they see in their clinical practice at Black Lion is rapidly increasing. They also both expressed that what they see is likely just the tip of the iceberg – most of the Crohn's patients they diagnose have severe disease that requires surgery, and there are undoubtedly many undiagnosed and misdiagnosed Crohn's patients in Ethiopia. Dr. Yohannes estimated that he has cared for 100-200 IBD patients at Black Lion, most of whom were diagnosed with Crohn's. Dr. Rezene estimated that most of their Crohn's patients (85%) would be categorized as lower-middle class, with 5% each in the extremely poor, poor, and rich/upper-middle class categories. ■

**Top: Endoscopy suite at Black Lion Hospital. Bottom: Manual scope cleaning using three-bucket system at Black Lion Hospital.**



# Ethiopia

## Saint Paul's Hospital, Addis Ababa August 22, 2019

Saint Paul's Hospital is a large public teaching hospital also located in Addis Ababa with two impressive endoscopy suites, and is the first African endoscopy center accredited as a World Endoscopy Organization (WEO) and European Society of Gastrointestinal Endoscopy (ESGE) training site. The two endoscopy suites are supported through partnerships with groups in Egypt and, and more recently Japan. Both are equipped for basic endoscopy and colonoscopy, and the newer unit has ERCP, but it is not yet functional. St. Paul's was the only facility we visited in Africa with an automated endoscope reprocessor, but it is not used. As with providers at Black Lion,

Dr. Haile reported an increase in IBD cases in recent years, and suspects there are many undiagnosed patients in Ethiopia due to poor awareness by both providers and patients. He emphasized that St. Paul's hospital typically sees Addis' poorest patients and estimated that the majority of his Crohn's patients (75%) would be categorized as poor or extremely poor, in contrast to the largely lower-middle class population seen at Black Lion. Dr. Haile and his team at St. Paul's have started to collect data on their cohort of Crohn's disease patients and noted that there is currently no national data or publications on the burden of Crohn's or IBD in Ethiopia.

In addition to gastroenterologists at St. Paul's, we had the opportunity to meet with a medical intern at Saint Paul's Hospital, who was also is also a Crohn's disease patient, Dr. Fasika Teferra. She was diagnosed while in medical school and considered quitting until she found support in a U.S.-based Facebook group for patients with Crohn's. This has inspired her to create a similar Crohn's support group in Addis online and on messaging apps and is hoping to eventually expand outside of Addis. We were very impressed by her initiative and hope there is a way we can support the work she is doing for Crohn's patients in Ethiopia. ■



**Top left: Automated endoscope reprocessor at St. Paul's Hospital. Top right: Endoscopy suite at St. Paul's Hospital. Bottom left: From left to right, Dr. Edom (medical intern), Dr. Fasika (medical intern), Neil Gupta (co-investigator), Ruma Rajbhandari (co-PI), and Samantha Smith (project manager) at St. Paul's Hospital. Bottom right: WEO/ESGE accreditation plaque at St. Paul's Hospital.**

# Ethiopia

**Teklehaimanot General Hospital, Addis Ababa**  
**August 22, 2019**



The third and final hospital we visited in Addis was the private Teklehaimanot General Hospital. The endoscopy suite here was considerably smaller than the previous two we had seen, with only one procedure room, and three scopes all together (two upper endoscopes and one colonoscope). They also utilized the three-bucket system for reprocessing used scopes. Unlike the other two hospitals we visited, patients had to pay substantial out of pocket fees for endoscopic procedures: \$50

USD for upper endoscopy and \$70 USD for colonoscopy. Dr. Rezene reported that he is actively caring for approximately 15 IBD patients at Teklehaimanot, the majority of whom are diagnosed with Crohn's disease, and that he currently sees 1-2 new IBD patients per month. He estimated that the majority of his Crohn's patients are middle class and live in Addis. ■

**Top: Three bucket cleaning system at Teklehaimanot General Hospital. Bottom: Endoscopy equipment at Teklehaimanot General Hospital.**



# Rwanda

## University Teaching Hospital of Kigali (CHUK), Kigali August 23, 2019

The last stop of our Africa site visits was CHUK (“Shi-ash-ka”), in Rwanda’s capital city of Kigali. The endoscopy unit at CHUK, which had been set up through the support of gastroenterologists from Dartmouth Hitchcock Medical Center and Brigham and Women’s Hospital, consisted of one procedure room and a three-step scope cleaning area. We met two endoscopists at CHUK, Rwanda’s main gastroenterologist Dr. Benoit Seminega, and internist/

endoscopist Dr. Eric Rutaganda. Both providers reported not having seen a single case of Crohn’s disease in Rwanda, and only two cases of UC. During our visit to CHUK, we had the opportunity to observe several endoscopic procedures and got a very real insight into some of the challenges faced by gastroenterologists in resource-limited settings. During one colonoscopy, the only functioning colonoscope kept getting clogged, and because there was not a back-up,

the endoscopist and nurses had to try to fix the scope mid-procedure. The light on the colonoscope was also not functioning very well, yet the gastroenterologist persevered and completed the procedure. The nurses and doctors also deliberated about whether they should continue on with defective equipment or try to do the procedures as best as possible since a dozen or so patients had already prepped for their anticipated colonoscopies that day. ■

### Appendix 3.8 Summary of Africa site visitscountry

Facility name	Facility type	Location	Providers	# IBD	# CD	# Uppers /day	# Colons /day	Challenges
Queen Elizabeth Central Hospital	Public	Blantyre, Malawi	Dr. Peter Finch Dr. Patrick Noah	4	2	8-10	<1	<ul style="list-style-type: none"> <li>- Only one gastroenterologist in all of Malawi</li> <li>- Lack of endoscopic capacity outside of large central hospitals</li> <li>- Difficult diagnosis due to patients’ inability to afford histology</li> </ul>
Neno District Hospital	Public	Neno, Malawi		0	0	0	0	<ul style="list-style-type: none"> <li>- No endoscopy at district hospital level – long wait for patients to get into Queens</li> </ul>
Black Lion Hospital	Public & private	Addis Ababa, Ethiopia	Dr. Yohannes Birhanu Dr. Rezene Behre	~200	~130	8-10	4-5	<ul style="list-style-type: none"> <li>- Lack of a Crohn’s or IBD clinical data registry</li> <li>- Difficult diagnosis due to patients’ inability to afford histology</li> </ul>
Saint Paul’s Hospital	Public	Addis Ababa, Ethiopia	Dr. Hailemichael Desalegn Mekonnen	>100	50	8-10	4-5	<ul style="list-style-type: none"> <li>- Poor Crohn’s awareness among providers</li> <li>- Lack of trained pathologists</li> </ul>
Teklehaimanot General Hospital	Private	Addis Ababa, Ethiopia	Dr. Rezene Behre	15	10-12	5-7	1-2	<ul style="list-style-type: none"> <li>- Underdiagnosis due to assumption that IBD is rare in Ethiopia</li> <li>- General pathologist only – no access to GI pathologist</li> <li>- Lack of diagnostics (i.e., fecal calprotectin)</li> </ul>
University Teaching Hospital of Kigali (CHUK)	Public & private	Kigali, Rwanda	Dr. Benoit Seminega Dr. Eric Rutaganda	2	0	8-10	<1	<ul style="list-style-type: none"> <li>- Poor Crohn’s awareness among providers</li> <li>- Lack of endoscopy outside of large central hospitals</li> </ul>

