Inflammatory Bowel Disease
A Sub-Saharan African Perspective

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1938-2018

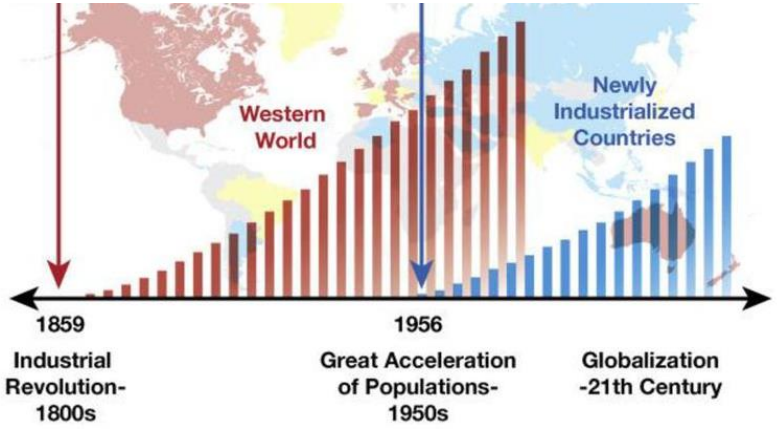
The Sub-Continent of Sub-Saharan Africa

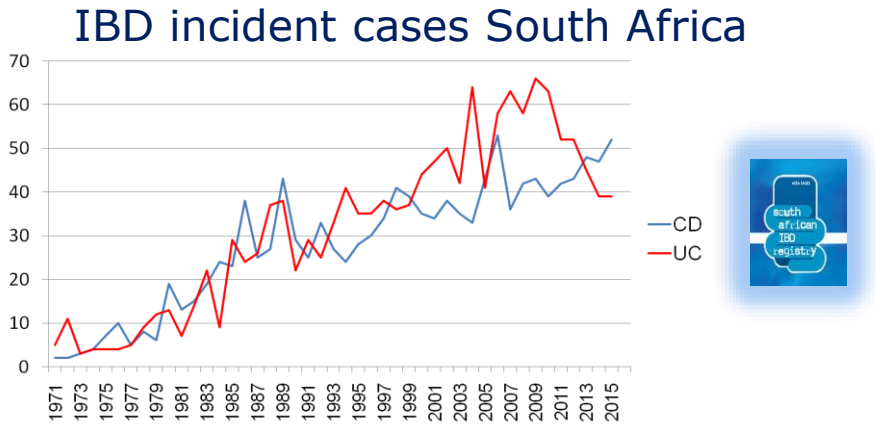
- Is made up of 46 countries, mostly situated south of the Saharan Desert
- Is home to 1.4 billion people
- Some countries have a reasonable economic outlook and political stability
- But the majority rank amongst the most impoverished in the World
- ➢ 19 of 20 poorest countries on the Globe are located in SSA

- Many have civil unrest
- Widespread political corruption
- With strained Health Care Services

- Impact the diagnosis and management of IBD in SSA

Global increase in IBD





- Outside of South Africa a diagnosis of IBD is still considered vanishingly rare
- This is well illustrated by a recent report from Cameroon
  - Where the authors summitted a case of CD
  - In order to highlight "this rare and curious entity"

Ng SC. Lancet. 2017;390:2769-78.
Dr David Epstein IBD Africa SA national registry
J Med Case Reports 2019:13,80

IBD in Sub-Saharan Africa

- A survey of endoscopists from 15 SSA counties
  - ➢ Ranked IBD as the least likely diagnosis they would encounter in practice.[1]

- Subsequently two systematic reviews published in 2020.[2,3]
  - ➢ Identified less than 250 published cases of IBD after excluding South Africa
  - ➢ Following the 1st report of CD from Rwanda in 1946.[4]

1 Hassan C. Endosc Int Open. 2018;6(10):E1247-e55

2.Watermeyer G. S Afr Med J. 2020;110:1006-9

3.Hodges P. International Health 2020;12:222–230

4. Kibaya A. East Afr Med J. 1946;23:317–320

IBD in Sub-Saharan Africa

- However the true burden of IBD is unknown as there is simply no data
- May be valid but the paucity of cases is likely due to other factors

➢ Missed diagnosis

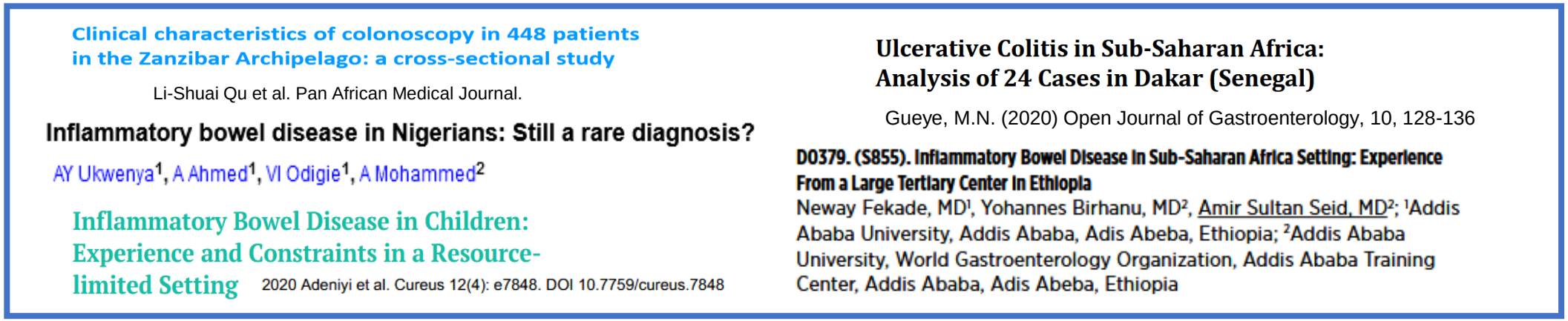
➢ Limited diagnostic capacity

➢ The widespread practice of Traditional African Medicine

➢ Under-reporting

Under-reporting of IBD cases in SSA

- Several initiatives have been introduced to heighten awareness of IBD in SSA
- Subsequently several case series, cross sectional studies have been published
- Adding significantly to the numbers identified in the systematic reviews



Clinical characteristics of colonoscopy in 448 patients in the Zanzibar Archipelago: a cross-sectional study

Li-Shuai Qu et al. Pan African Medical Journal.

Inflammatory bowel disease in Nigerians: Still a rare diagnosis?

AY Ukwenya[1], A Ahmed[1], VI Odigie[1], A Mohammed[2]

Inflammatory Bowel Disease in Children: Experience and Constraints in a Resource-limited Setting

2020 Adeniyi et al. Cureus 12(4): e7848. DOI 10.7759/cureus.7848

Ulcerative Colitis in Sub-Saharan Africa: Analysis of 24 Cases in Dakar (Senegal)

Gueye, M.N. (2020) Open Journal of Gastroenterology, 10, 128-136

D0379. (S855). Inflammatory Bowel Disease in Sub-Saharan Africa Setting: Experience From a Large Tertiary Center in Ethiopia

Neway Fekade, MD[1], Yohannes Birhanu, MD[2], Amir Sultan Seid, MD[2]; [1]Addis Ababa University, Addis Ababa, Adis Abeba, Ethiopia; [2]Addis Ababa University, World Gastroenterology Organization, Addis Ababa Training Center, Addis Ababa, Adis Abeba, Ethiopia

- One study from a single tertiary centre in Ethiopia
- Reported 104 cases of IBD, CD outnumbered UC by 2.5:1

IBD in Sub-Saharan Africa

Prospective data

- Since the inception of an IBD database 18 months ago
  - ➢ Over 200 incident cases identified across the sub-region
  - ➢ Likely an underestimation given that data entry is voluntary
- IBD in SSA may not be as rare as believed and is likely on the rise

Personal communication: Dr Phoebe Hodges, Zambia

- Outside of South Africa and Ethiopia the vast majority of cases are UC
  - ➢ In keeping with data from other regions
  - ➢ During the 1st stages of the epidemiological transition
  - ➢ With an initial emergence of UC followed later by an increase in CD

Kaplan G, Nat Rev Gastroenterol Hepatol. 2021;18:56–66

Missed Diagnosis of IBD

- One of the most plausible explanations for the rarity of reported cases
- Due to a very low index of suspicion
- And the high burden of parasitic infections that closely mimic IBD

➢ *Entamoeba histolytica*
➢ *Schistosoma mansoni*
➢ *Strongyloides stercoralis*

- All are endemic in SSA
- Although prevalence varies between and within countries

Parasitic Colitis

E histolytica, S mansoni, and S stercoralis
Can all present with symptoms that closely resemble IBD

- Chronic or intermittent bouts of diarrhoea (often bloody)
- Abdominal cramps, loss of appetite and loss of weight
- Anaemia

- Given the perceived rarity of IBD
- It is likely that many cases are mistakenly labelled as infectious entero-colitis

- Common practice for patients to receive multiple courses of metronidazole
- Before referral for further work up

Diagnosis of Parasitic enterocolitis

- The most widely available diagnostic test is stool microscopy
- Has poor sensitivity even with processing of multiple specimens
  - ➢ Trophozoites and cysts of Amoebiasis may not be detected
  - ➢ Ova of Schistosomiasis and larvae of Strongyloidiasis may be absent

- Serology is of little value in high prevalence areas
  - ➢ Cannot discriminate current from past infection

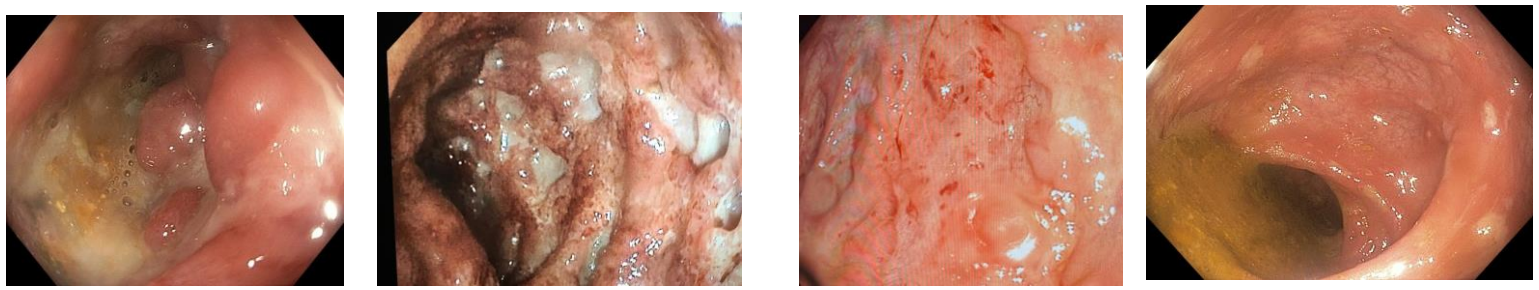
- Stool antigen testing and PCR are generally unavailable

- Peripheral eosinophilia suggests a parasitic infection but can be seen in IBD

Click B. Am J Gastroenterol. 2017;112:1849-1858

Endoscopic features of Parasitic colitis

- Highly variable
- Range from relatively normal mucosa to non-specific colitis, or atypical lesions
- Some cases can closely resemble UC or CD

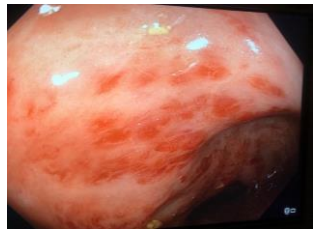


Amoebic colitis

- Deep caecal ulcers with exudate and rectal involvement if sexually transmitted
- Less commonly the mucosa demonstrates a uniform, diffuse colitis

Endoscopic features of Parasitic colitis



S mansoni

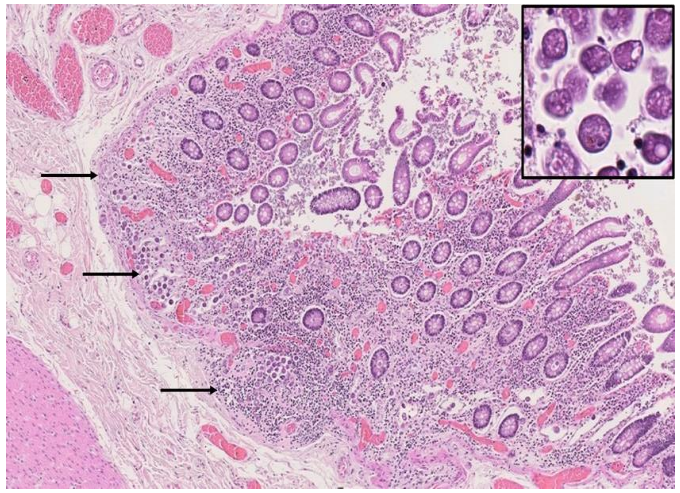
- Infects the left colon
- With strictures and polyps
- Can mimic CD


Strongyloides stercoralis

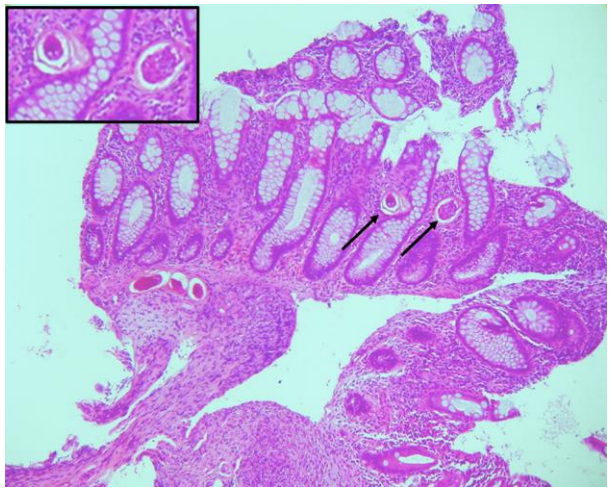
- Caecal ulceration
- If there is more extensive colitis:
  - ➢ Rectum often spared with skip lesions
  - ➢ Can be mistaken for CD
- But can present as diffuse pan-colitis

Histopathology is necessary to make a diagnosis

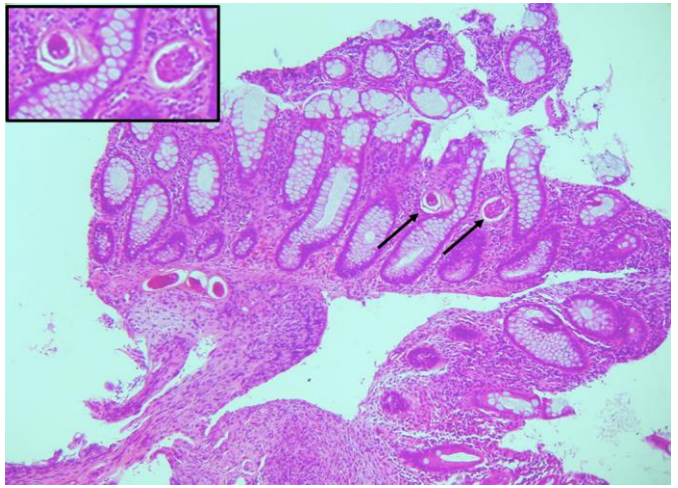
- To identify a parasitic infection or to rule one out before diagnosing IBD



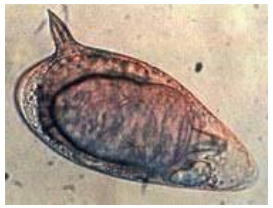
Trophozoites of *E histolytica*



Ova of *S mansoni*



Nematodes of *S stercoralis*



Watermeyer G. Lancet Gastroenterol Hepatol. 2022 ;7:952-961.

Getting the diagnosis right

- Missing IBD will result in a delay in initiating effective IBD medications
  - ➢ With a risk of disease progression and development of complications

- Mislabelling a parasitic colitis as IBD can have devastating consequences

- Parenteral corticosteroids can:
  - ➢ Precipitate a toxic megacolon and perforation in Amoebic colitis
  - ➢ Trigger *S stercoralis* hyperinfection syndrome which is often fatal

Watermeyer G. Lancet Gastroenterol Hepatol. 2022 ;7:952-961.

Very high rates of *M tuberculosis infection*

- An important consideration in diagnosing IBD in SSA

- Differentiating Intestinal tuberculosis from Crohn's disease is challenging
- Many overlapping clinical, endoscopic, radiographic, histological features

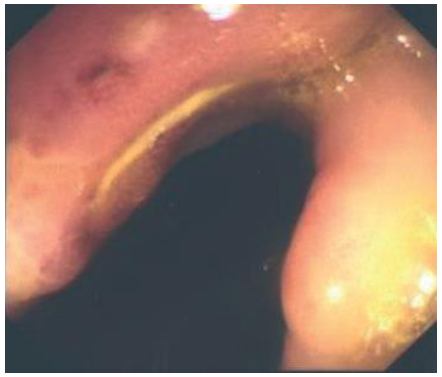
- A definitive diagnosis of ITB requires one of the following on tissue biopsy:
  - Caseating granulomas
  - Presence of acid-fast bacilli
  - Positive tissue GeneXpert MTB rifampicin (RIF) assay/TB PCR
  - A positive TB culture

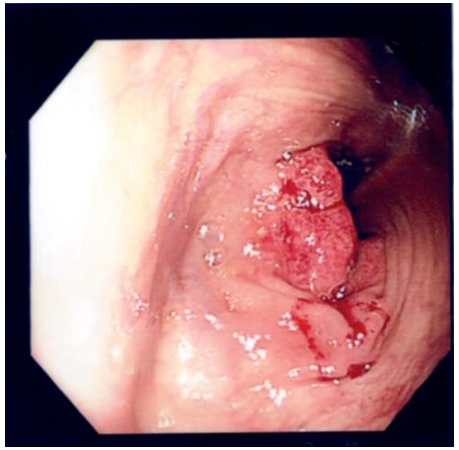
- These findings are present in fewer than 30% of cases of ITB

	Features favouring CD	Features favouring ITB
Clinical	Positive IBD family history Perianal disease Extra-intestinal manifestations	Positive TB contact Night sweats Ascites
Laboratory		Strongly positive TST Strongly positive IGRA Positive HIV test
Radiographic	Presence of the comb sign Mesenteric fibro-fatty proliferation Ileum > caecum	Destruction of the caecum

Endoscopic features of Intestinal Tuberculosis

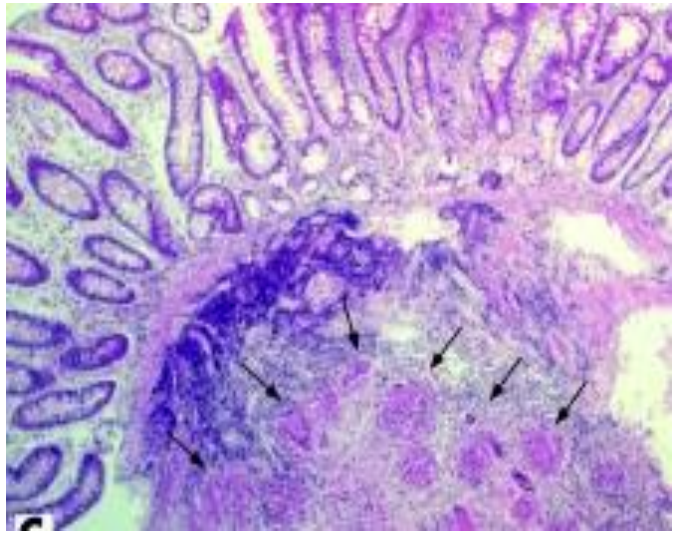
- Transverse ulceration
- Patulous ileocaecal valve
- Pseudopolyps
- Tumour like lesions



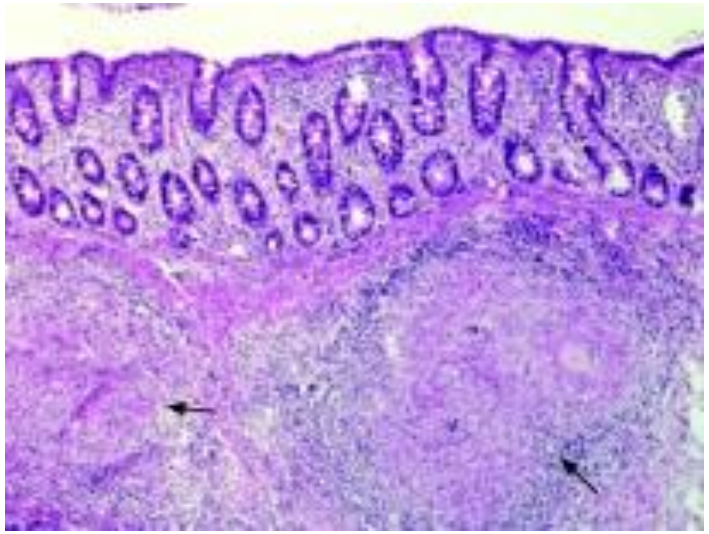


Watermeyer G. Lancet Gastroenterol Hepatol. 2022 ;7:952-961.

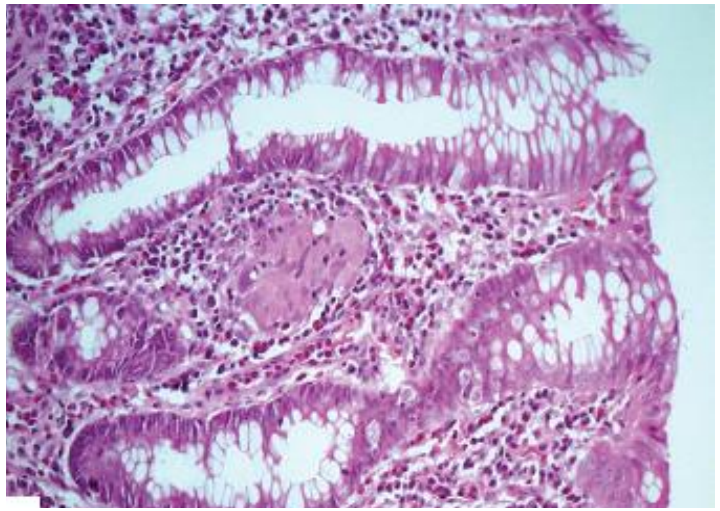
Histopathology of Intestinal Tuberculosis vs. CD



Intestinal TB
Multiple sub-mucosal granulomas
Well formed
May be confluent

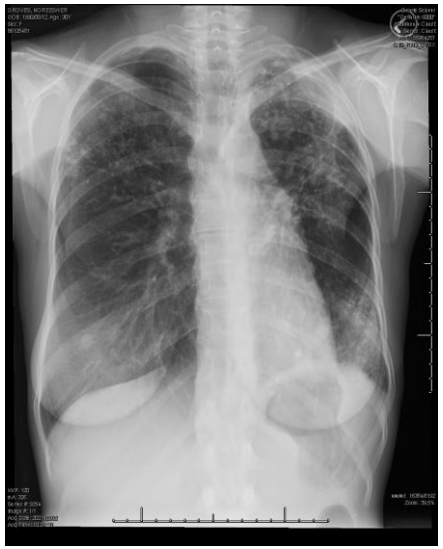


Intestinal TB
Large sub-mucosal granulomas

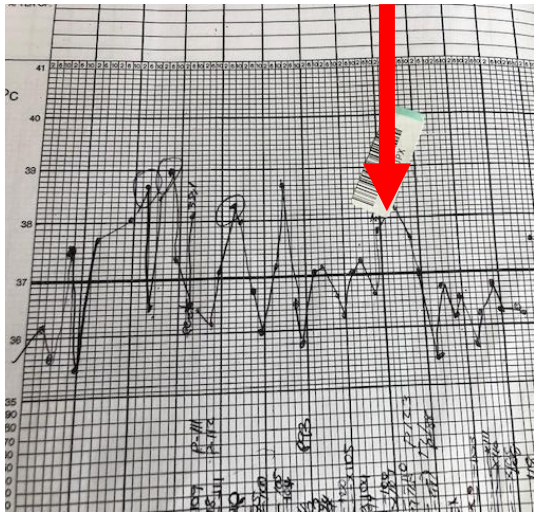


Crohn's disease
Single, small granuloma
Poorly formed

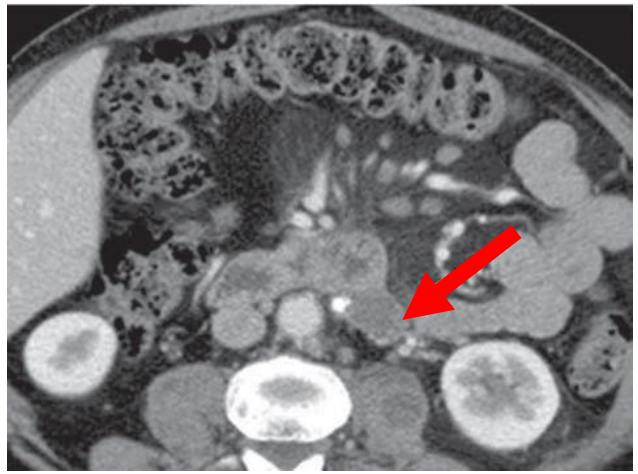
Features favouring ITB in my practice



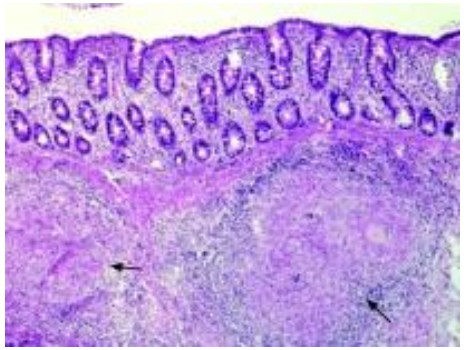
CXR
Features of previous TB



Swinging fever
Response to ATT



Lymph nodes larger than 1 cm
Central hypoattenuation



Multiple, well formed granulomas

Getting the diagnosis right

- Incorrectly labelling IBD as Intestinal TB
  - ➢ Can result in disease progression
  - ➢ Empiric anti-TB therapy in CD is associated with the development of strictures

Gupta A, J Crohns Colitis. 2020;14(11):1611-1618.

- However missing ITB
- Treating with anti-TNFs increases the risk of life threatening dissemination

- Generally err on the side of ITB
  - ➢ With an empiric trial of anti-TB therapy
  - ➢ Assess response after 2 months

Limited diagnostic capacity

- Another plausible explanation for the paucity of reported cases
- ➢ Is limited diagnostic capacity across much of the sub-region

Statement 1.1. ECCO-ESGAR Diagnostics GL [2018]

A single reference standard for the diagnosis of CD or UC does not exist. The diagnosis of CD or UC is based on a combination of clinical, biochemical, stool, endoscopic, cross-sectional imaging, and histological investigations

- Most sub-Saharan Africans cannot access these diagnostic modalities
- Especially endoscopy, cross sectional imaging, and anatomical pathology
- These are virtually non-existent in rural areas

*Maaser C. Journal of Crohn's and Colitis 2019;*13,144–164

A critical shortage of specialists

- One of the main factors negatively impacting service delivery

- A recent survey reported 1.2 endoscopists per 1 000 000 population.[1]
  - Ranging from 1 per 400 000 people to 1 per 2 million people

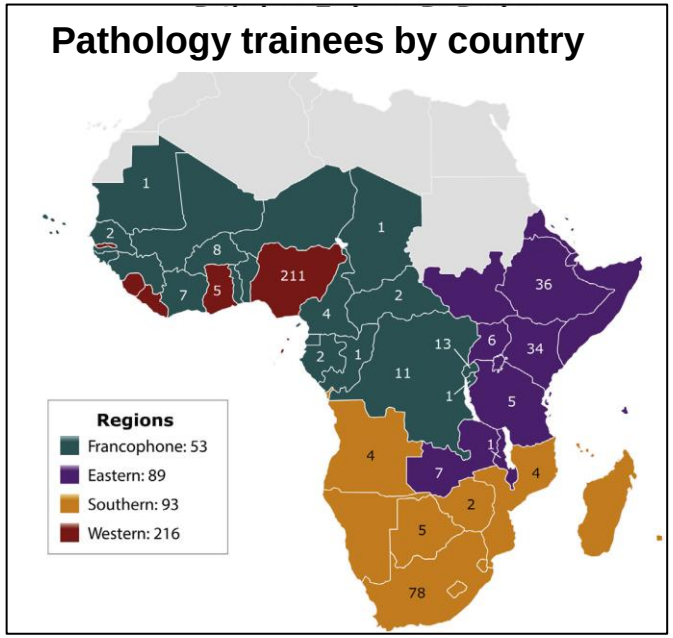
- On average, there is one pathologist for every million people in SSA.[2]
  - Concentrated in Nigeria, Ghana, Kenya, Ethiopia, Uganda, and Tanzania
  - The majority are in South Africa

- Radiologists are also in short supply.[3]
- South Africa fares best with one radiologist per 60 000 people
  - In the rest of SSA range from one per 350 000 people to 1.4 million

1. Mwachiro M .Endosc Int Open. 2021;9:E1827-E36. 2 .0Iyawe EP. SA J Radiol. 2022;26:2347
3 .Fleming K. Ecancermedicalscience 2019;13: 945.

Countries with Post-graduate Programs

Country	Year estimated	Number of Radiologists
Cameroon	2017	50
Ethiopia	2012	100
Ghana	2020	56
Kenya	2020	146
Nigeria	2020	355
Rwanda	2020	11
South Africa	2020	659
Sudan	2020	30
Tanzania	2020	60
Uganda	2020	50



- Despite dedicated residency programs, numbers of specialist are relatively low
- This may reflect inadequate capacity to train larger numbers of specialists
- Also, a consequence of the 'Brain Drain"

0Iyawe EP. SA J Radiol. 2022;26;:2347
Nelson AM,. Clin Lab Med 2018; 38: 37–51

The ‘Brain Drain’

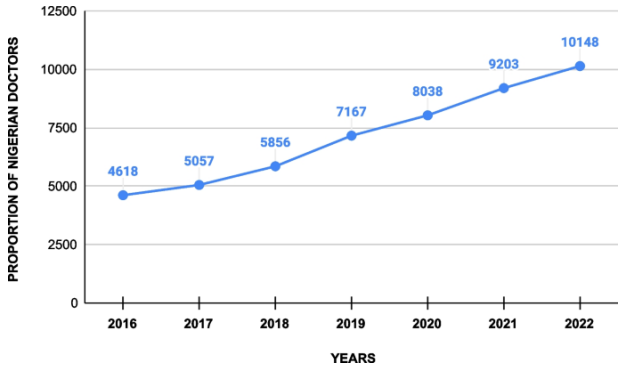
- Migration of Health Care Professionals
  - From LMIC in SSA to high income regions in search of greener pastures
  - Also internally with migration from the public to private care health sector

- Major push factors are
  - Poor standard of living, quality of life, and low salaries
  - Limited access to advanced technology, education, and research opportunities
  - Political instability and fears for personal safety

- This is a longstanding problem but has escalated since the onset of COVID
  - Due to COVID related corruption and exposure of deficiencies in Health Care

The Brain drain in Nigeria

- Nigeria, the most populous country in SSA, is one of those most affected
- The 'Giant of Africa" is losing specialist at an alarming rate
- The main destinations are the UK, USA, Canada, Australia, and Saudi-Arabia
- In a recent publication only 110 endoscopists were practising in Nigeria
- With a population of 213 million people



According to a UK government report
13,609 HCWs left Nigeria for the UK in 2022
An exponential rise

Lawal L .Int J Equity Health 2022; 21,17, Onah C.Hum Resour Health 2022;20,85, Kamarulzaman A. Lancet 2022; 29:492-1494
Asombang AW. Niger J Gastroenterol Hepatol 2022;14:49-54

Limited Diagnostic Capacity

- Due to unavailability of equipment: CT and MRI scanners, and endoscopes
  - ➢ With numbers woefully short to provide adequate diagnostic services.[1-3]
  - ➢ Notably the public sector, where equipment is often outdated or malfunctioning

- More advanced technology is limited to the private sector
  - ➢ Difficult to access due to cost and lack of health insurance
  - ➢ Subject to high rates of out-of-pocket expenditure

- Little local capacity for repairs. Most countries do not have formal contracts.[2]
  - ➢ Damaged equipment is sent to other countries at exorbitant expense

1. Anazodo UC. NMR Biomed 2022; 19:e4846. 2. Hassan C. Endosc Int Open. 2018;6(10):E1247-e55. 3. Ngoya PS.Pan Afr Med J 2016;25:99

Abdominal Ultrasound in SSA

- 43% of participants at a WGO workshop reported having access to USS.[1]
- Still mostly performed by Radiologists and Radiographers

- But POCUS is rapidly being adopted by non-radiologist clinicians in SSA.[2]
  - ➢ Mostly for Obstetric indications
  - ➢ Increasingly being used by Emergency care Physicians

- Given increasing accessibility and reduced cost
  - ➢ POCUS is the obvious solution to fill the cross-sectional imaging gap in IBD
  - ➢ Currently some USS training is included in 47% of GI training programs.[3]
  - ➢ Data on its use in luminal Gastroenterology is lacking

1.Perl D. Afr Health Sci. 2016;16:329-38. 2.Wanjiku G.BMC Health Serv Res2018;18: 607

3.Personal communication Prof Akwi Asombang

Electricity as a barrier to service delivery

- SSA is the least powered region in the world,
- 600 million people live without electricity especially in rural areas

- Even for those who do have access to the grid, supply is often unreliable
- Load shedding is in place in many countries

➢ Especially problematic in Zambia, Zimbabwe, South Africa

➢ In South Africa most major Tertiary hospitals are exempt

➢ But this is not the case in rural hospitals and in many other countries

- Without alternative power, prolonged outages cripple diagnostic services

➢ With a knock on effect for cold chain capacity, travel, and education

Traditional African Medicine (TAM)

- May delay or obscure the diagnosis of IBD

- Traditional healers are often the 1st step in the health-care pathway
- Especially in rural areas
- Treatments range from spiritual interventions to herbal remedies

- The widespread use of TAM reflects
  - ➢ Limited access to Western style health institutions
  - ➢ Cultural beliefs
  - ➢ Convenience (100 traditional healers for every university trained doctor)
- Traditional healers are an indispensable part of Health Care Services
  - ➢ But unlikely that their skill set extends to diagnosing and managing IBD

Traditional African Medicine (TAM)

- 4 studies have reported the use of TAM in the management of diarrhoea

- In a study from Kenya:
  - 97% of participants had used herbal preparations as 1st line therapy.[1]
  - And the majority purposely chose TAM over allopathic medicine

- Many will receive care from both TAM and the Western health care sectors
- A practice known as medical pluralism.[2]
  - Has been shown to contribute to delays in diagnosis in persons living with HIV
  - As well as delays in the implementation of effective therapy

1.Njoroge GNnya). African Journal of Ecology [Internet]. 2007;45(s1):65–70. 75
2.Moshabela M. Sex Transm Infect. 2017;93(Suppl 3)

Availability of IBD medicines in SSA

- Once a concrete diagnosis of IBD is made, further challenges lie in store

- In particular access to IBD medications which is limited in many countries
- There is a heavy reliance on corticosteroids and 5-ASAs

- Given limited availability of more expensive therapies in many SSA countries:
  - Steroids are often used as long-term maintenance treatment
  - 5-ASAs (invariably salazopyrine) are used to treat most patients with CD

  - Azathioprine and methotrexate are available
  - But use is limited by inconsistent accessibility and procurement barriers

Watermeyer G. Lancet Gastroenterol Hepatol. 2022 Oct;7(10):952-961

Availability of Advanced IBD Therapies

- Anti-TNFs are formally registered in only a handful of countries
- Use is hugely skewed to the private sector often requiring OOP payments

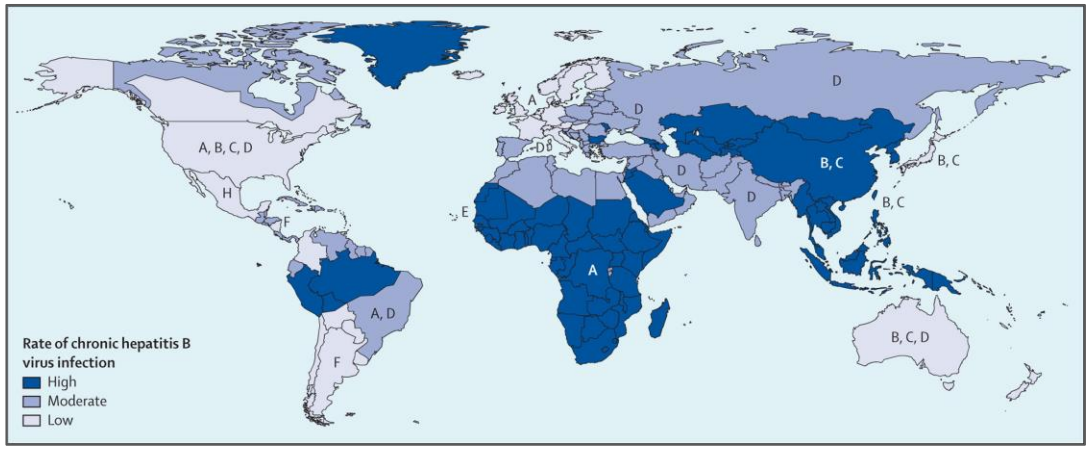
- In South Africa public sector access is still on a named case-by-case basis
- Elsewhere uptake of anti-TNFS in the public sector is virtually non-existent

- Other advanced therapies such as ustekinumab, vedolizumab, and tofacitinib
  - ➢ Are prescribed in a few countries, mostly in South Africa
  - ➢ Use is exclusively in the private sector

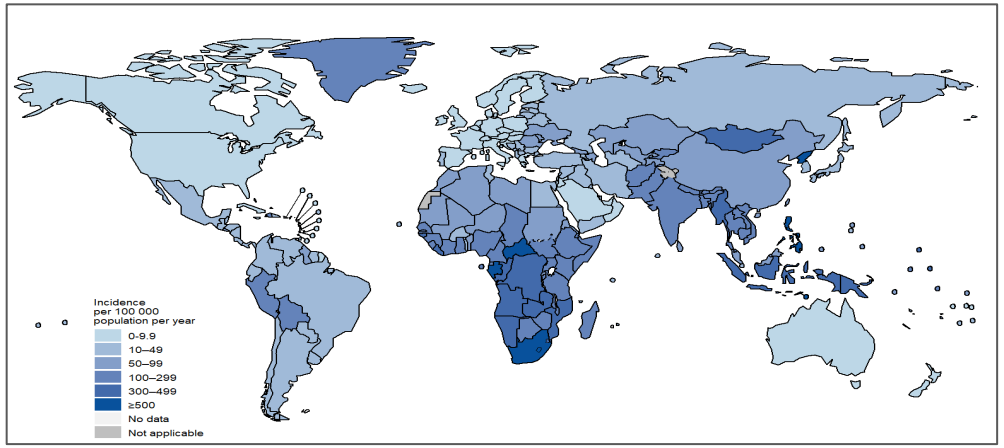
Watermeyer G. Lancet Gastroenterol Hepatol. 2022 Oct;7(10):952-961

Latent Tuberculosis and Chronic Hepatitis B

- For patients lucky enough to access anti-TNFs there are further challenges
- High rates of latent tuberculosis and Hepatitis B infection
- Anti-TNFs are a risk factor for reactivation



Chronic Hepatitis B



Incidence of TB per 100 000 population

Trépo C. Lancet. 2014;;3842053-63. *https://www.who.int/publications/digital/global-tuberculosis-report-2021/tb-disease-burden/incidence*

The best time to plant a tree was 20 years ago
The next best time is now
African proverb

- Many initiatives have been introduced to address these short comings

- Mostly directed at the broader fields of Radiology, Pathology, Gastroenterology

- For Gastroenterology the focus is primarily on building endoscopic capacity
- Usually involves a collaboration between
  - ➢ A local facility and one from a high resource area
  - ➢ Or partnership with an International society

- There are a few that focus specifically on IBD

Non-profit organisations from South Africa

IBD Africa: champions patient education and advocacy across SSA

- Has become the voice of IBD patients across the region
  - ➢ Hosts regular online meetings
  - ➢ Their website has extensive educational resources in multiple languages
  - ➢ Social media footprint reached more than 21,000 people in 2022

GHASSA: focuses on continued medical education of SSA Gastroenterologists

- Partnered with Project ECHO, University of New Mexico
  - ➢ IBD-GECHO was launched to heighten awareness and improve IBD care
  - ➢ With regular virtual meetings with colleagues from 15 SSA countries

Sub-speciality GI training in SSA

- Less than 50% of countries have GIT sub-specialization programs
- Fellows are trained in high income countries and often do not return

- It is key to establish local capacity to provide formal GI specialization
- Successfully achieved in Zambia
- Where there was no capacity to train Gastroenterologists
  - ➢ University of Zambia successfully initiated a GI MMED program in 2016
  - ➢ With the 1st graduate in 2020
- Demonstrating that such a model is achievable in a low resource setting

Personal communication Prof Paul Kelly

*https://www.unza.zm/academics/*postgraduate-programmes/master-of-medicine-gastroenterology-and-internal-medicine-taught

Digital Health Technology in SSA

- SSA has been dubbed ‘the new breeding ground for digital global health’
- Teleradiology and Telepathology
  - ➢ Ideal solutions to circumvent the shortage of specialists
  - ➢ However attempts to implement programs have failed to gain traction
  - ➢ Due to infrastructure (limited access to PACS,WSI) and power outages

- Widespread availability of mobile technology has changed that
- 67% of people in SSA have mobile devices, about half are smart phones
- Vast majority of Doctors have access to smartphones with 4G or 5G networks
- Easily send images for evaluation and 2nd opinions with reasonable accuracy

Holt C. Lancet Digital Health 2020

Ntja U. Afr J Emerg Med. 2022;12(1):67-70

Artificial intelligence

- In the future AI could potentially be a game changer in SSA

- Will assist endoscopists and pathologists with limited IBD experience
  - ➢ In diagnosing IBD, grading severity, detecting dysplasia

- Interpret CT, MRE, and USS automatically with AI image recognition systems

- May finally solve the ITB vs. CD dilemma
  - ➢ Once reliable and functional clinical decision support tools are available
  - ➢ Small studies have already showed benefit in discriminating ITB from CD

Kim JM. Gastroenterol Hepatol. 2021;36:2141

The perfect opportunity for IBD research

- SSA is undergoing rapid urbanization
- Her cities are the fastest growing in the world
- With a median age of 20 years, is the youngest population in the world

- SSA appears to be one of the last regions on the globe to:
- Enter the early stages of the IBD epidemiological transition

- There is untapped potential to perform research
- While the increase in cases is still in its infancy and most are biologic naive
- In many regions the opportunity to study 'early days' of IBD has long passed

Why is IBD on the rise in SSA?

- Changes in diet?
  - SSA is experiencing a rapid nutritional transition
  - Moving away from the traditional African diet to a more westernized diet
  - Foods high in sugar, saturated fats, emulsifiers, and preservatives

Bosu WK. The Proceedings of the Nutrition Society. 2015;74:466-477

- Pollution?

- Changes in the microbiome and the Hygiene hypothesis?
  - Wide-spread eradication of *H pylori*
  - Population eradication programs for Schistosomiasis and Helminth infections
  - More regular exposure to antibiotics

Setshedi M, Watermeyer G. Front Med (Lausanne). 2022;9:1013779

Conclusion

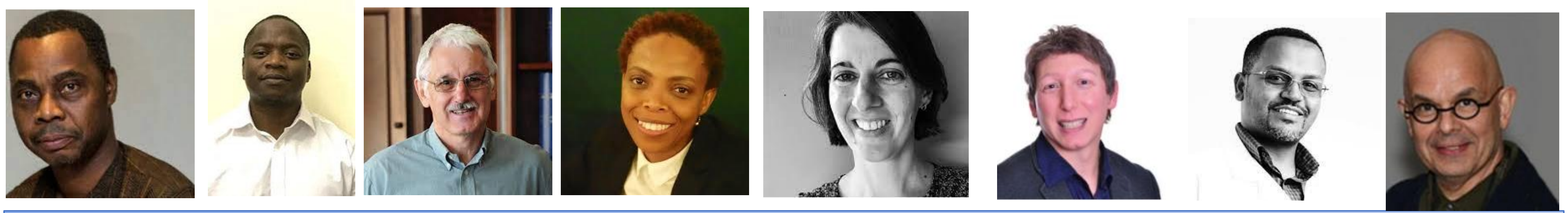
- IBD has certainly reached the shores of SSA and is likely on the increase

- While there are many challenges in diagnosing and managing IBD in SSA
  - The many initiatives that have been introduced will go a long way
  - In increasing diagnostic capacity and availability of medications

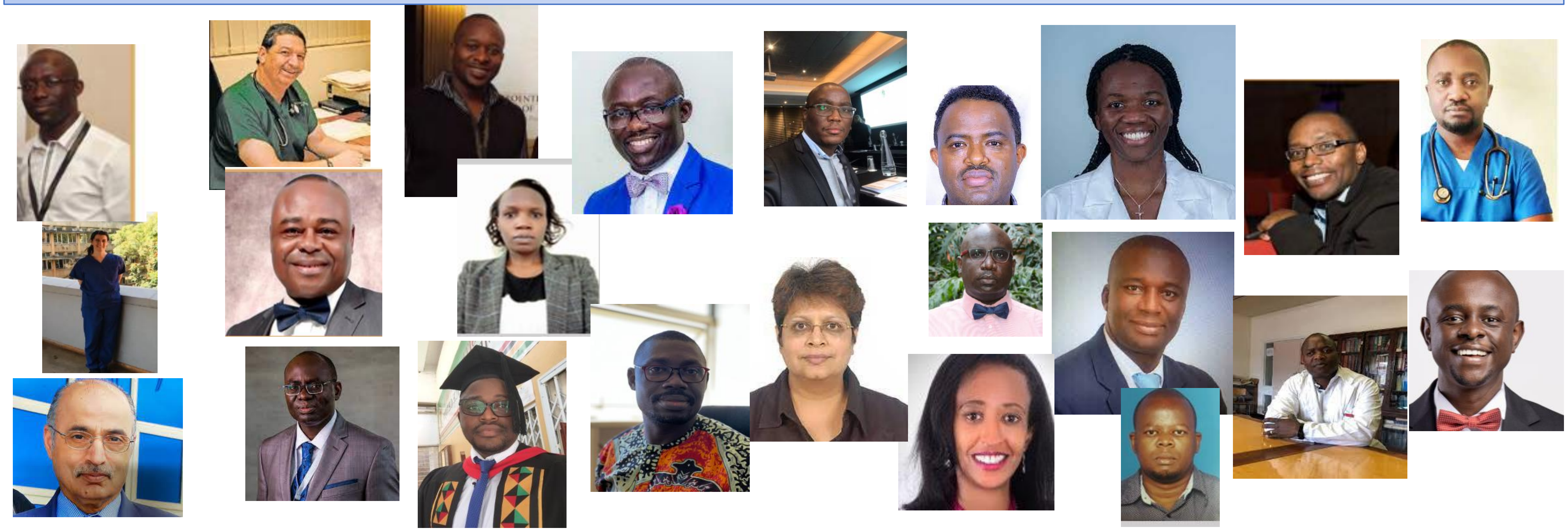
  - In the future digital technology and AI will be game changers

- At this point in time heightening awareness of IBD in SSA is key
  - Among patients and healthcare workers across the board

- With this the future of IBD in SSA is getting a little brighter every day



My thanks to all my colleagues from across SSA




Nkosi Sikelel' iAfrika
God Bless Africa
The National Anthem of South Africa