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The African Research Group for Oncology (ARGO): technology and cancer in low- and middle-income countries

Isaac Alatise, MD, WACS
Professor, Dept. of Surgery
Obafemi Awolowo University Teaching Hospital

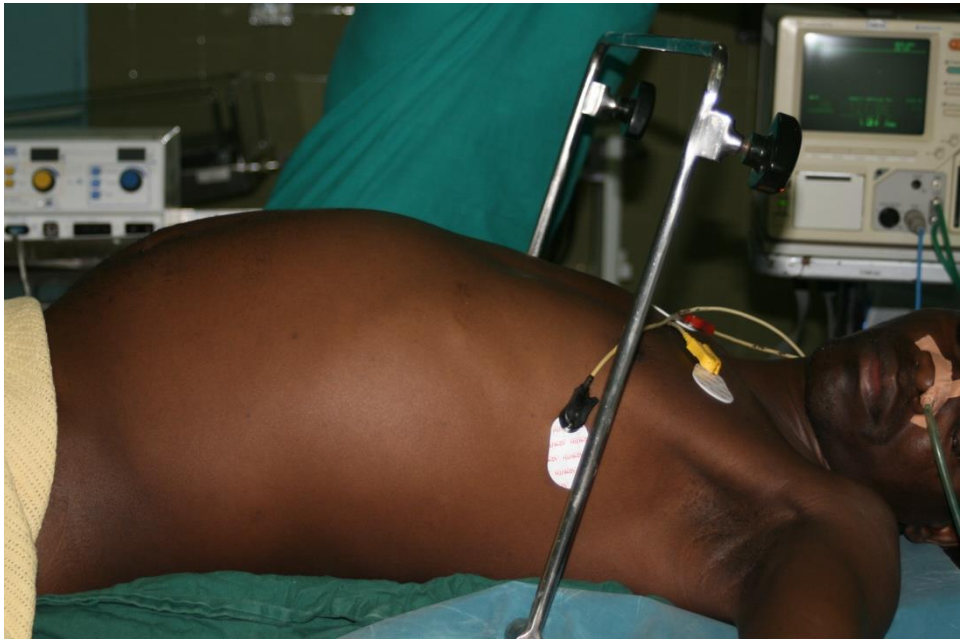
T. Peter Kingham, MD, FACS
Director, Global Cancer Research and Training Program
Professor, Hepatopancreatobiliary Surgery
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- No conflicts

Cancer is a growing problem in Low- and Middle-Income Countries (LMIC)

- By 2050, 70% of the predicted people with cancer in LMIC

- Lancet Oncology Commission on Global Cancer Surgery: majority of cancer patients require surgical intervention



Kingham TP, Alatise OI, et al. *Lancet Oncology* 14:e158-167 (2013)
Sullivan R, Alatise OI, et al. *Lancet Oncology* 16(11):1193-224 (2015)

"Obesity Was Rising as Ghana Embraced Fast Food. Then Came KFC."



The New York Times

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Why does this matter to us?

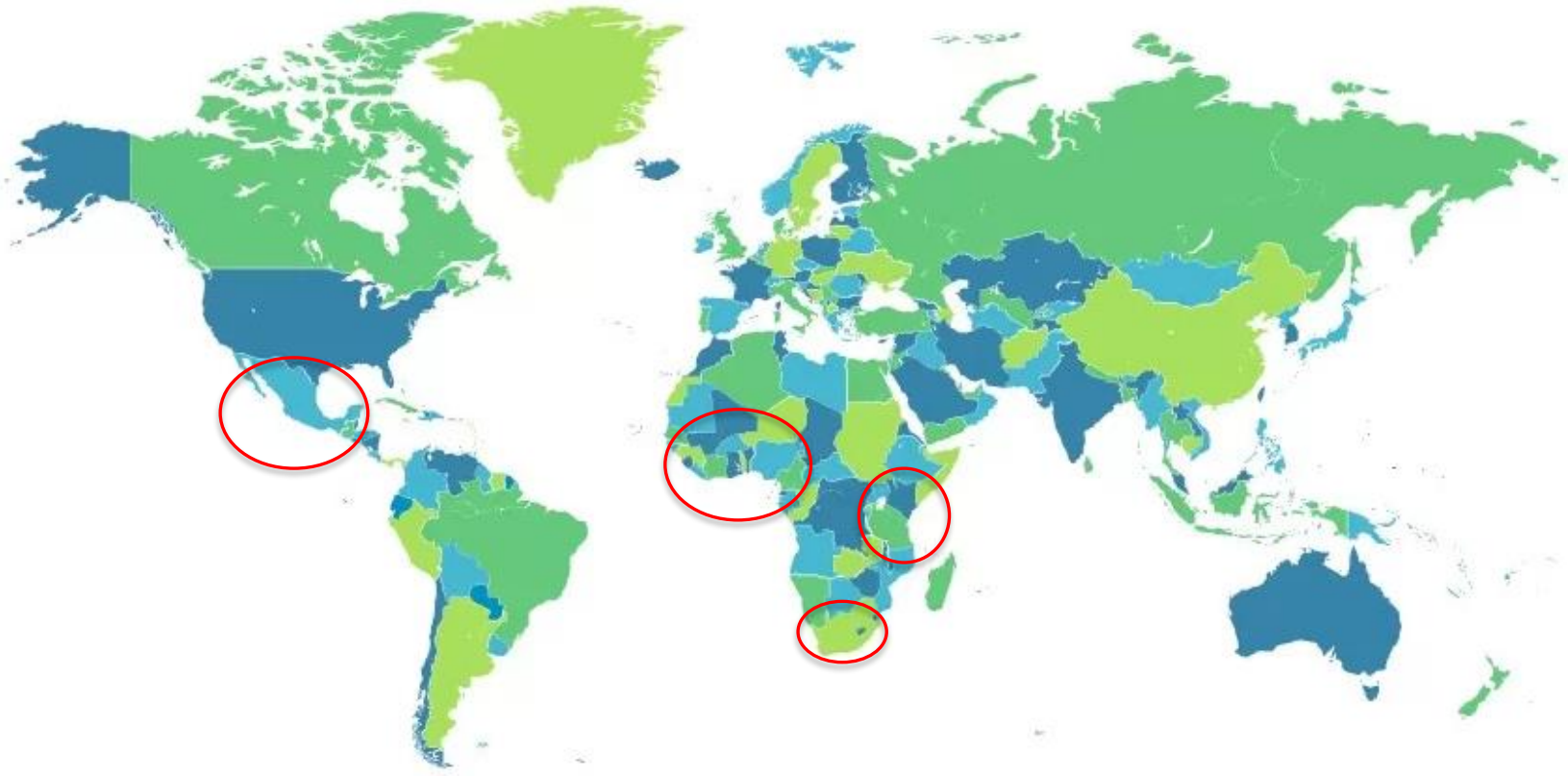
- We cannot understand the biology of cancer by studying cancer regionally
- As cancer rates rise globally, we can learn about overcoming screening/early diagnosis barriers
- We will learn about environmental and cultural impacts on cancer by studying in LMIC
- Cancer research in LMICs is cost effective

MSK Global Cancer Research and Training (GCRT) Program

To improve *outcomes* for cancer patients in sub-Saharan Africa using collaborative research and training efforts.

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GCRT active collaborations



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GCRT spans all Departments at MSK

- Clinical focus:
  - Cancers:
    Breast/CRC/Cervix/Gastric/Sarcoma/Lung
  - Psycho-oncology; Palliative Care; Nursing

- 20 active faculty members
- 6-person research/admin team at MSK
- 50-person research/admin team in Nigeria

African Research Group for Oncology: Academic collaborative model

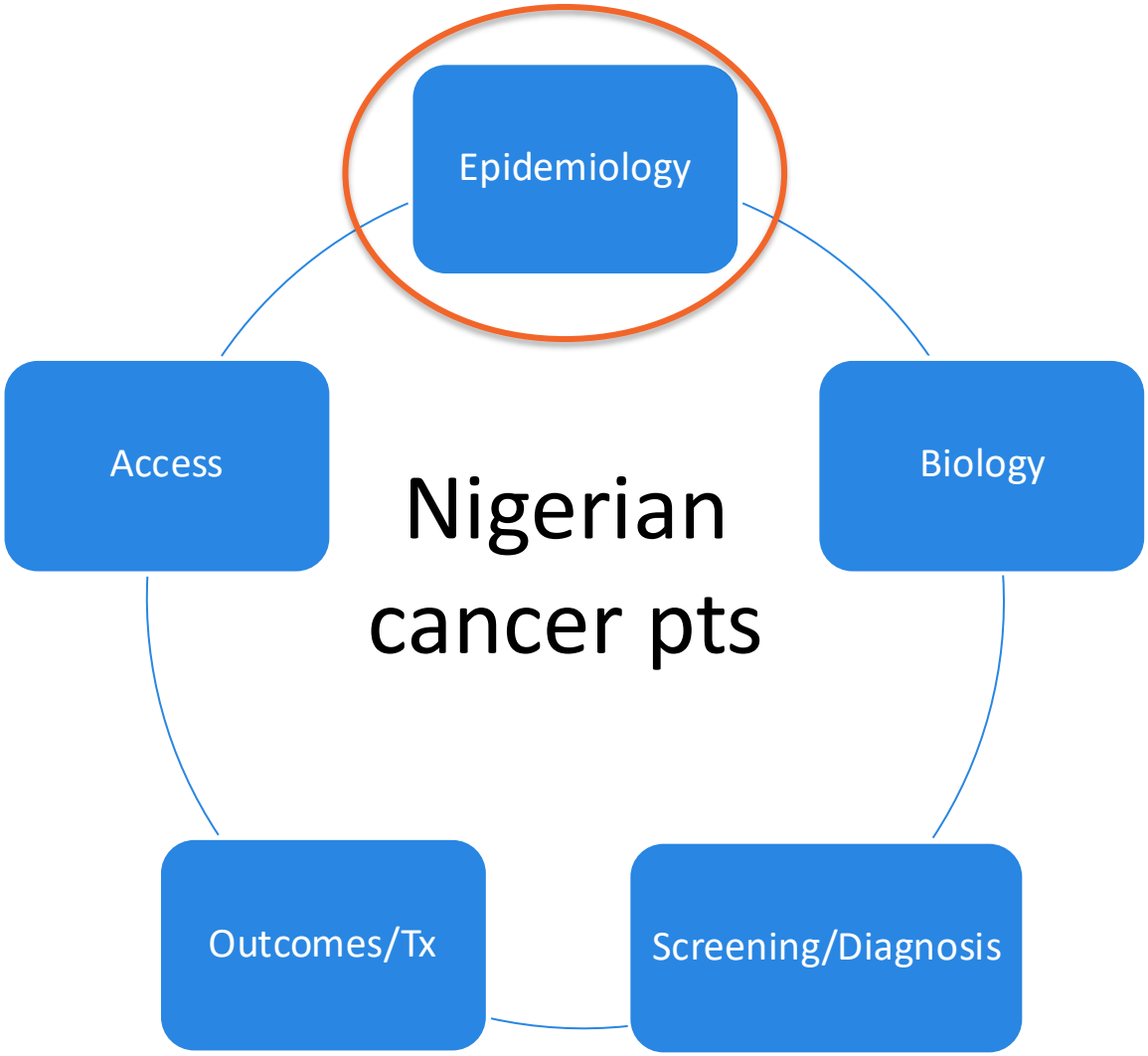


ARGO
African Research Group for Oncology
National Cancer Institute (NCI)
Approved Colorectal Cancer Consortium
In Collaboration with
MSKCC USA



Fischer SE,...Kingham TP. *Annals of Surgical Oncology* 24(3):627-31 2016

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Epidemiology
Biology
Screening/Diagnosis
Outcomes/Tx
Access
Nigerian cancer pts

CRC patients present late in Nigeria

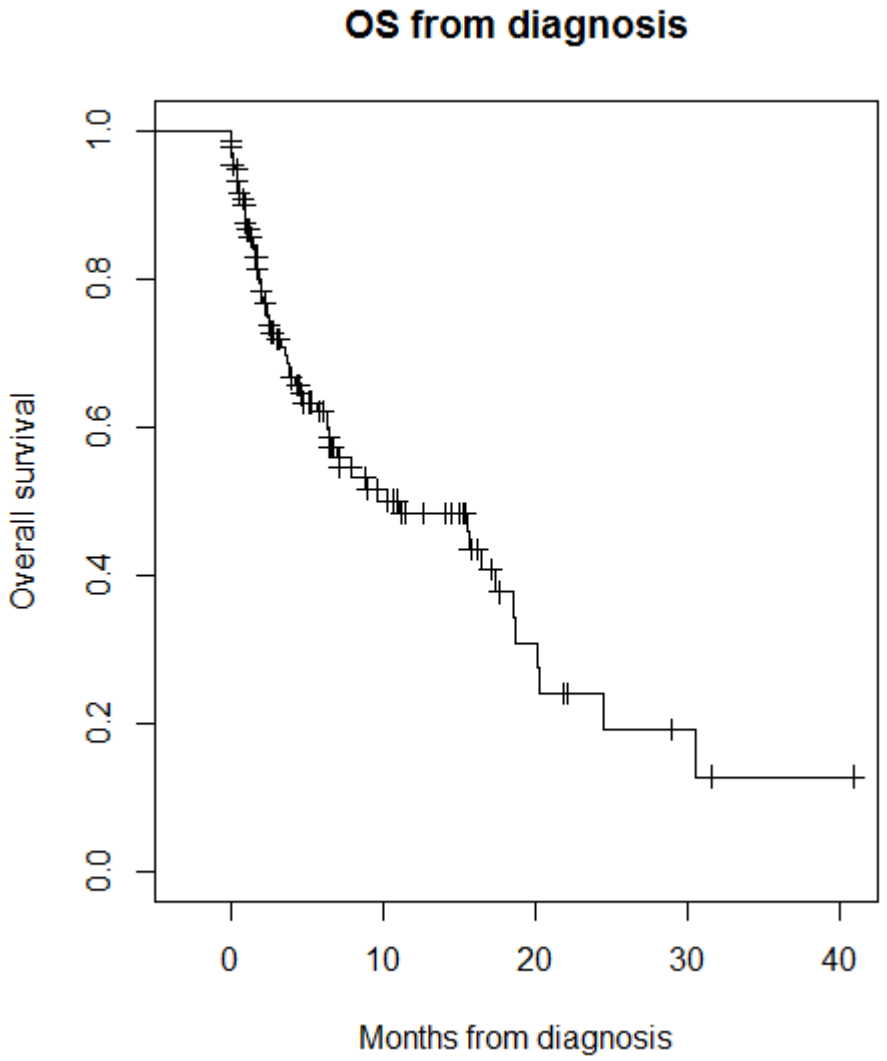
Stage	% Nigeria (n=380)	% USA (SEER)
I	.3%	39%
II	13%	36%
III	34%	-
IV	54%	20%



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Survival in patients with CRC in Nigeria is poor

- 6-month survival: 62.6% (95% CI: 53.6-72.1)
- 12 month survival: 48.4% (95% CI: 38.9-60.1)



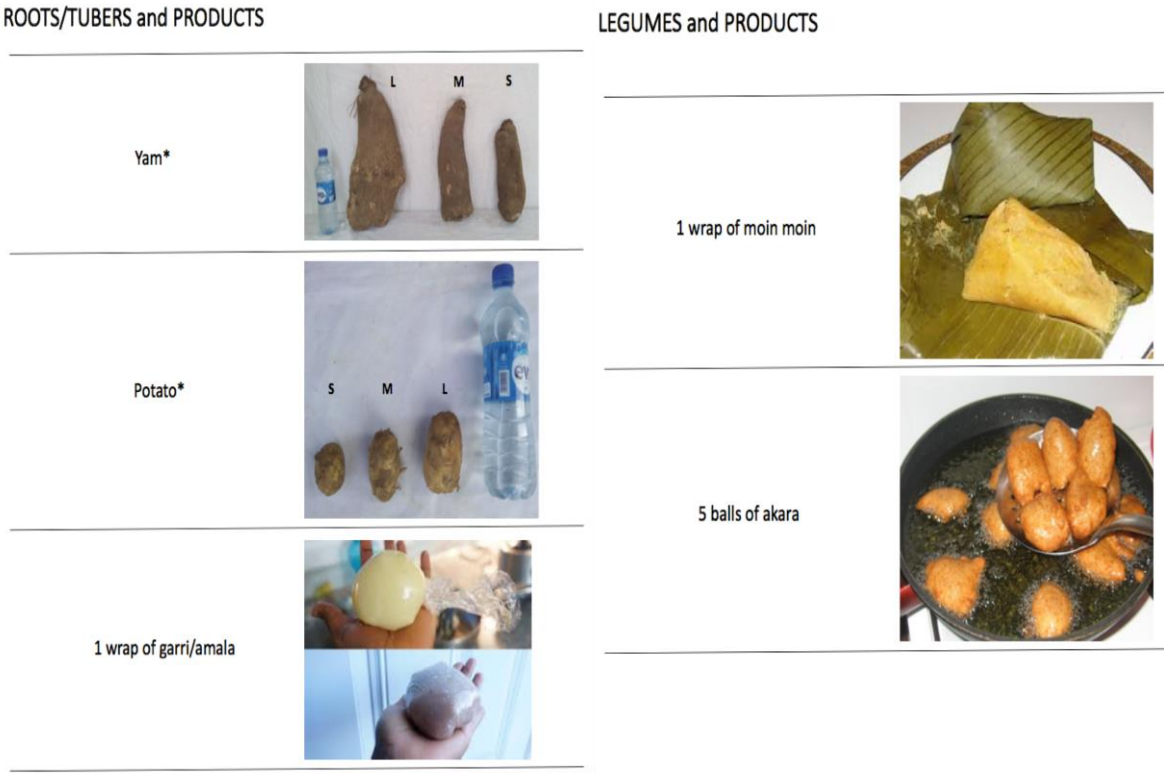
What are risk factors for cancer in Nigeria?





What are risk factors for cancer in Nigeria?

- Diet and exercise assessment based on Nurses Health Study[1]
- Validation with food diaries and photo documentation of meals[2]



[1]Hu et al. *Am J Public Health* 106(9):1567-1572. 2016
[2]Peeri N et al, *Cancer Causes and Control*. (in press 2023)
Funded by NCI R01 (Kingham, Alatise)

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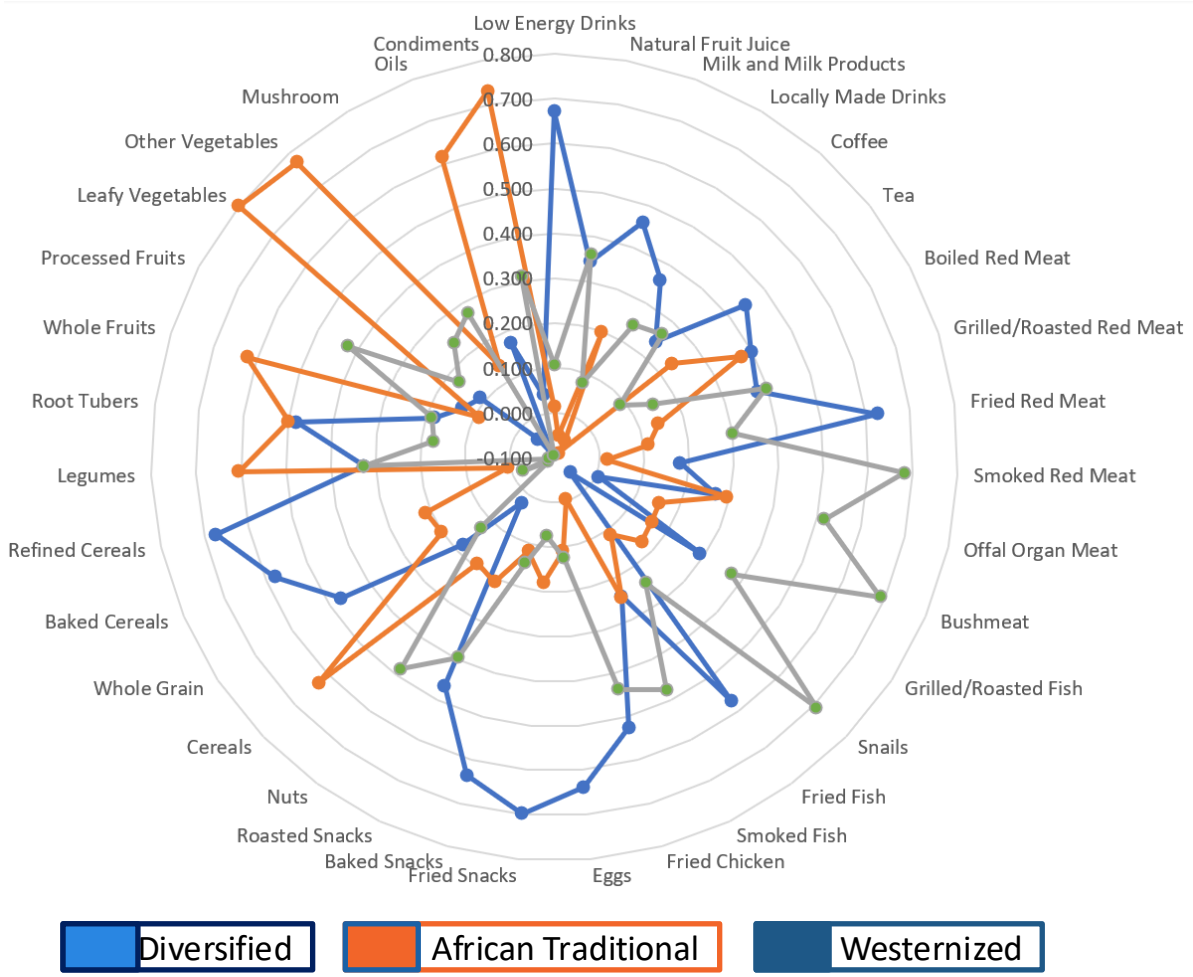
Dietary Patterns (DP) and CRC

- Studies on diet and CRC have mostly been carried out in HIC
- Sub-Saharan African studies focused on isolated nutrients/food types, but people tend to eat in patterns

Methods

- Case-control study with 507 cases and 1114 controls in Nigeria, West Africa
- 3 empirical DPs (using principal component analysis):
  - Diversified: Wide range of food groups
  - African traditional: Fruits and vegetables dominated
  - Westernized: Processed/red meat dominated

Westernized DP increased CRC risk in all models and stratifications of analysis

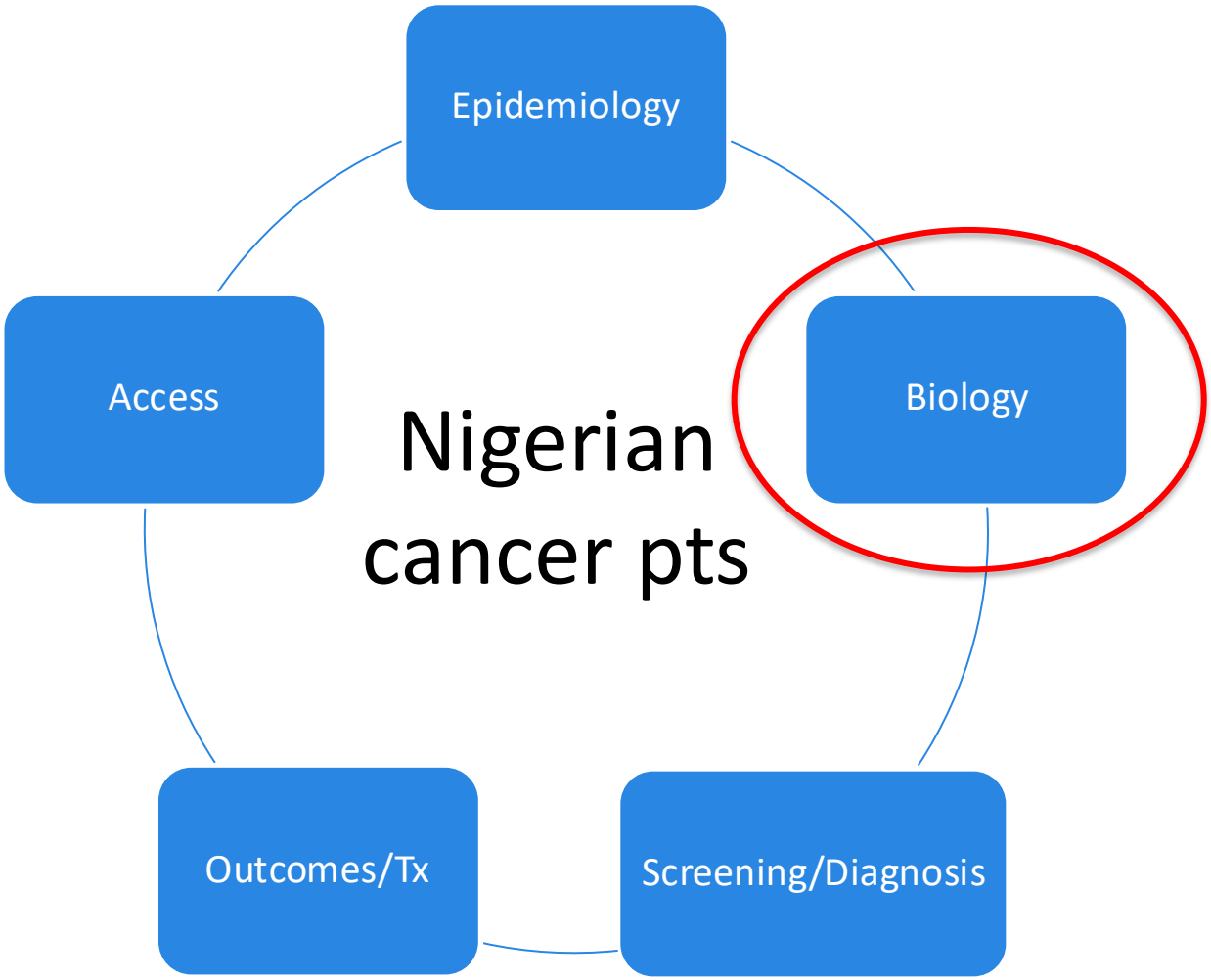


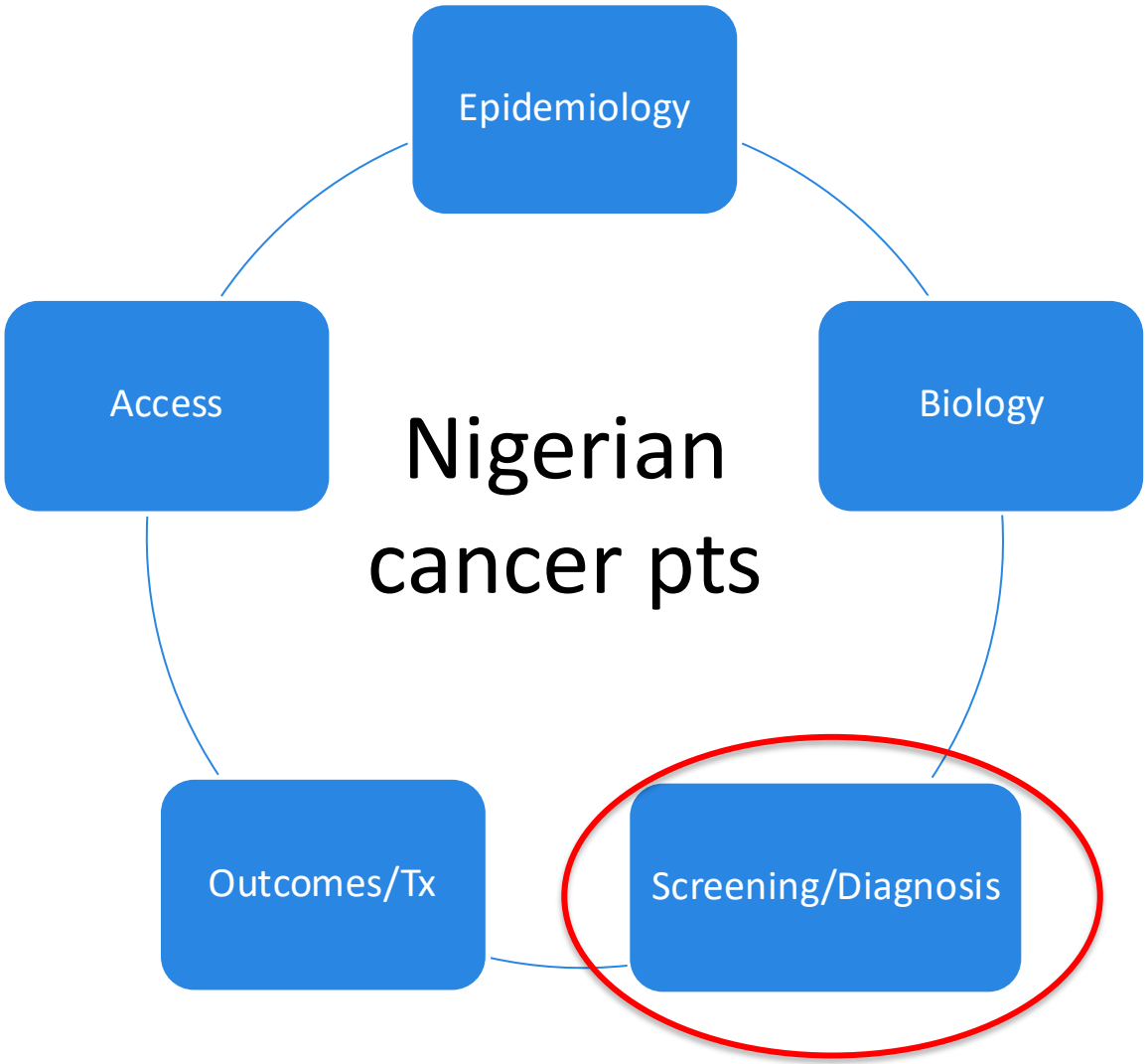
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Exploratory analysis of association between chemical compounds exposure and CRC risk

Compound Class	N Cases	N Controls	OR	95% CI
Organosphates				
Low	9 (36%)	17 (65%)	Ref	Ref
High	16 (64%)	9 (35%)	4.74	1.34, 19.5
Polycyclic Aromatic Hydrocarbons				
Low	10 (40%)	17 (65%)	Ref	Ref
High	15 (60%)	9 (35%)	6.12	1.58, 29.1
Pesticides				
Low	11 (44%)	19 (73%)	Ref	Ref
High	14 (56%)	7 (27%)	3.24	0.85, 13.5

*A sum score was created to reflect the number of chemicals within a compound class that a participant was exposed to. We split exposures using the median value for each chemical compound class.
Adjusted for age, sex, education.


Epidemiology
Biology
Screening/Diagnosis
Outcomes/Tx
Access
Nigerian cancer pts



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Approaches for screening/early dx for CRC in Nigeria

No prospective trials of any CRC screening or early dx method in sub-Saharan Africa

- Is it feasible?
- High-risk groups ideal

	Average risk	First degree relatives	Symptomatic
FIT	X	X	
Clinical screen			X
Urine metabolites		X	X
Blood methylation panel		X	X

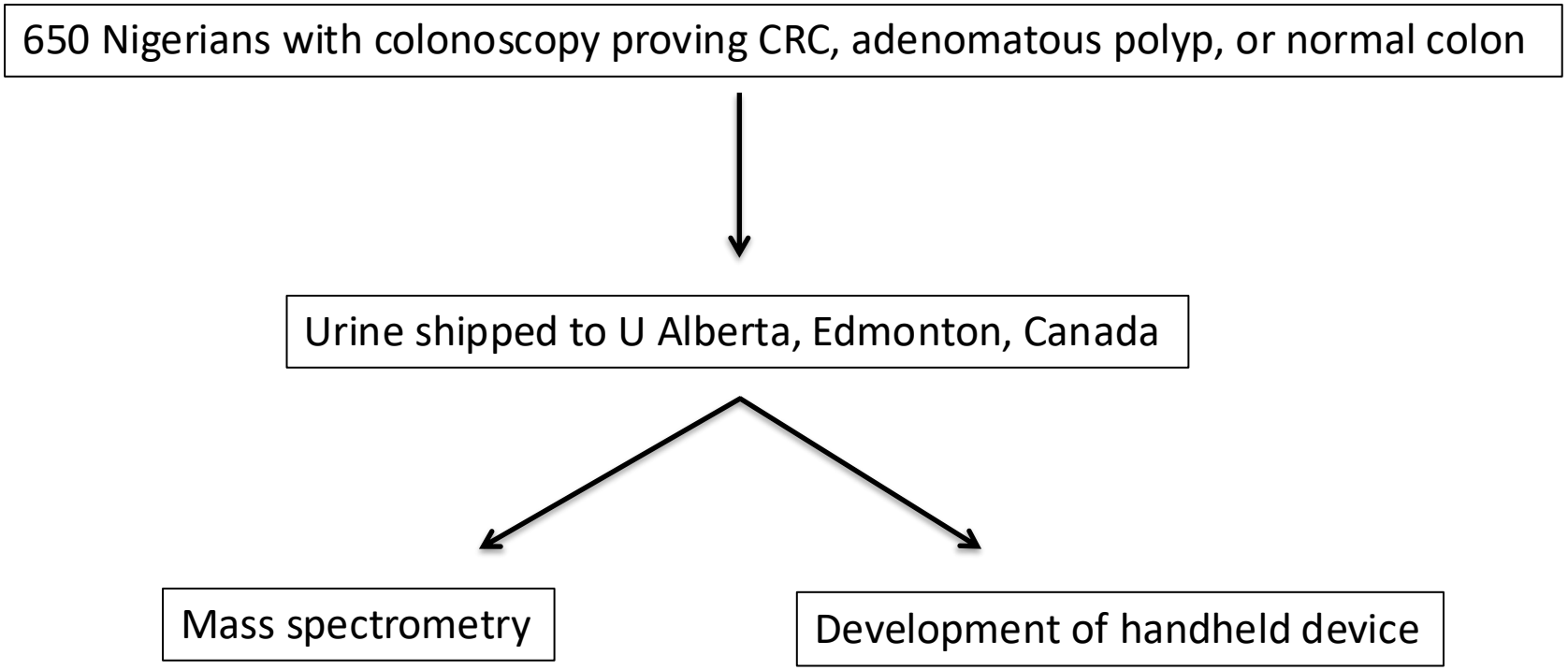
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Knapp G.,…, Kingham T.P. World Journal Surgery. 2019 Nov; 43(11):2674-2680

Should tests that work in HIC work in LMICS?

- What can affect a cancer diagnostic test's performance in LMIC?
  - Environment – for test and for cancer
  - Cost
  - Differences in biology
  - Health systems differences
    - Is implementation possible?????
  - Who should lead implementation?

Can we diagnose polyps/CRC with urine metabolites?

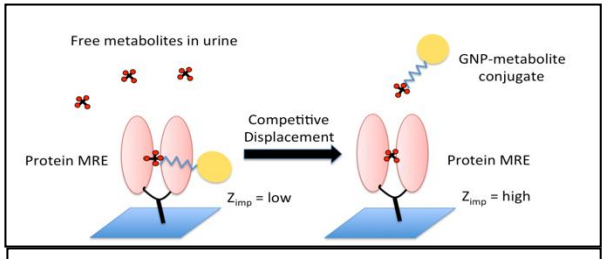


Kingham, Alatise JGO 2025; supported by NCI UG3/UH3 grant

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Timeline of technology development

- 2016 NIH UG3/UH3
  - 2 years UG3
  - 4 years UH3
- Applied with 3 metabolites that ended up not working
- Applied with an impedance-based model
  - Competitive assay and change in impedence measured



Timeline of technology development

- Nigerian patients did not match the known metabolites
- The impedence system didn't work
- Our co-PI leading the engineering team tragically died

- 6-year project became 8-year project and was only 60% completed

Metabolites are associated with CRC dx

- Mass spectrometry used to quantify 142 metabolites in urine from 514 Nigerian CRC patients and healthy controls

- Diacetylspermine, hydroxyhippurate, and glutamate best metabolites in Nigerian patients

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Zhang L et al. Cancer Biomarkers. 2023; 36(1): 17-30

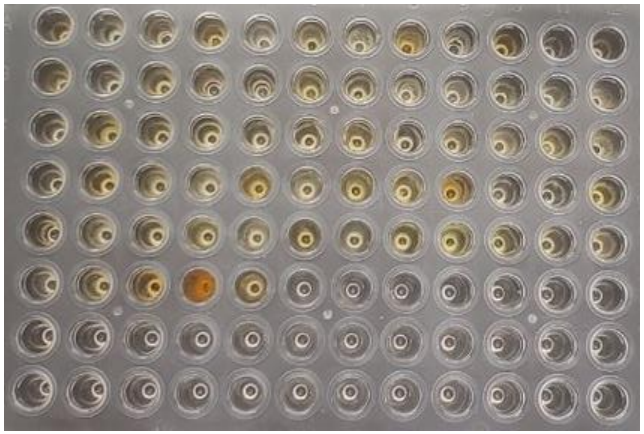
Nigerian patients with clinical factors added to Diacetylspermine

Inputs	Sensitivity	Specificity	AUC
Diacetylspermine	87%	50%	0.803
Diacetylspermine + Weight Loss	94%	50%	0.856
Diacetylspermine + Blood in Stool	90%	50%	0.822
Diacetylspermine + Weight Loss + Blood in Stool	94%	50%	0.858
Weight Loss (yes or no)	81%	67%*	0.739

*Since we are using only yes and no for the clinical features, we don't have a point where the specificity is 50%.



Nigerian samples dilution:



Assay:



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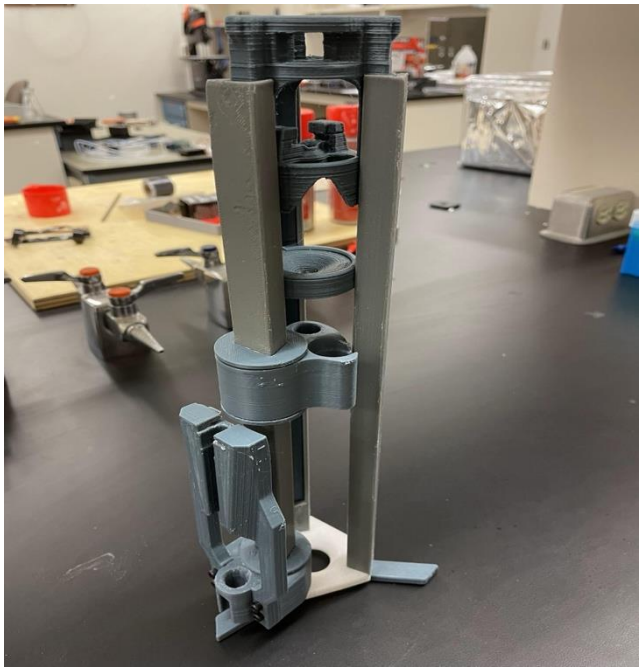
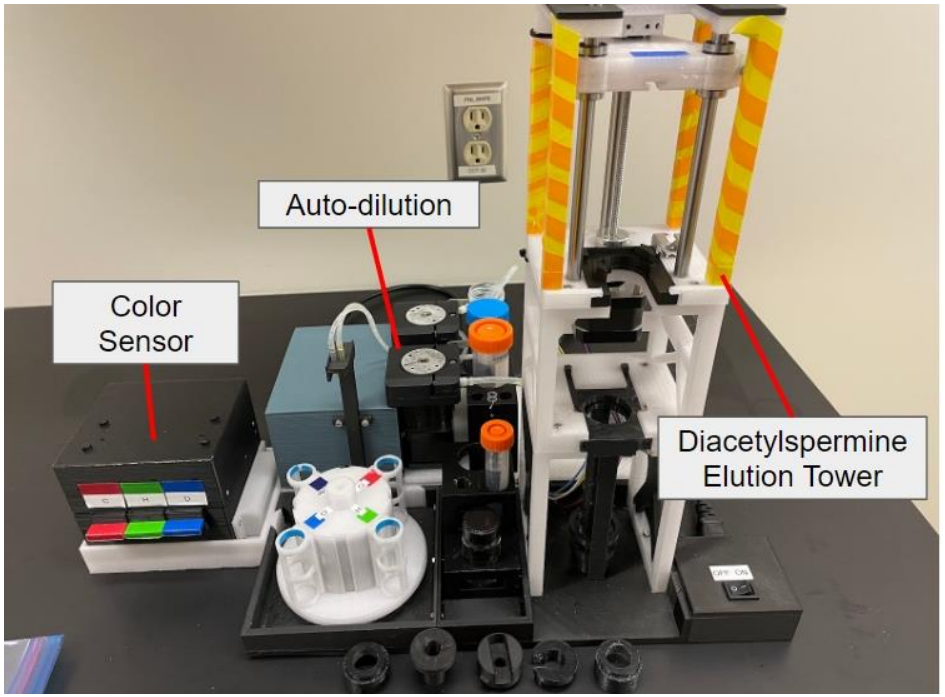
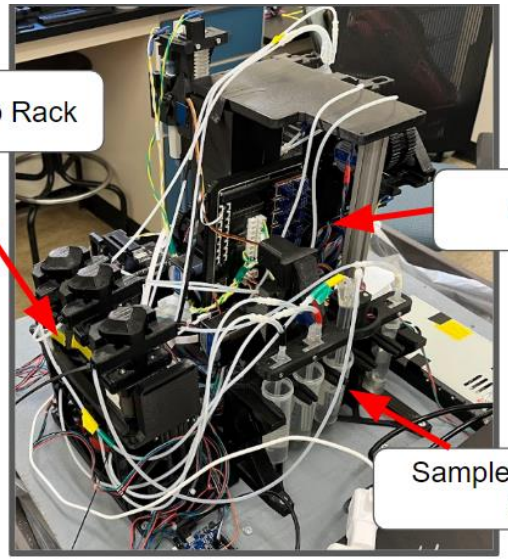
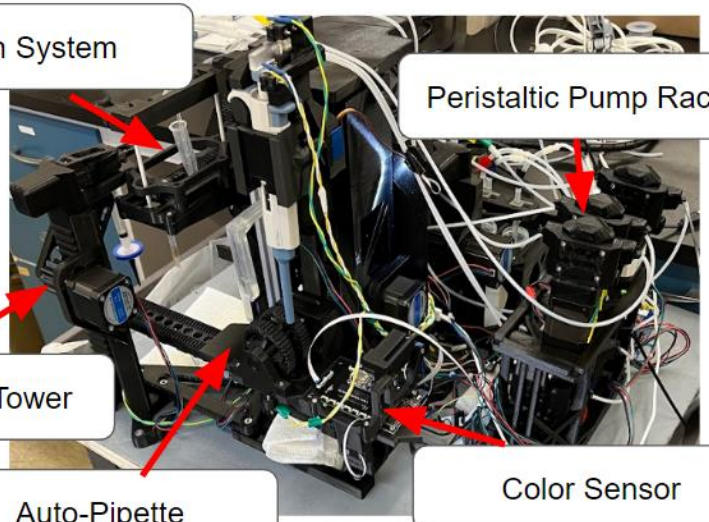


Figure 1: Manual filtration setup with 3D printed assistance structures




Peristaltic Pump Rack
Control Board
Sample and reagent input


Elution System
Peristaltic Pump Rack
Syringe Filter Tower
Auto-Pipette
Color Sensor

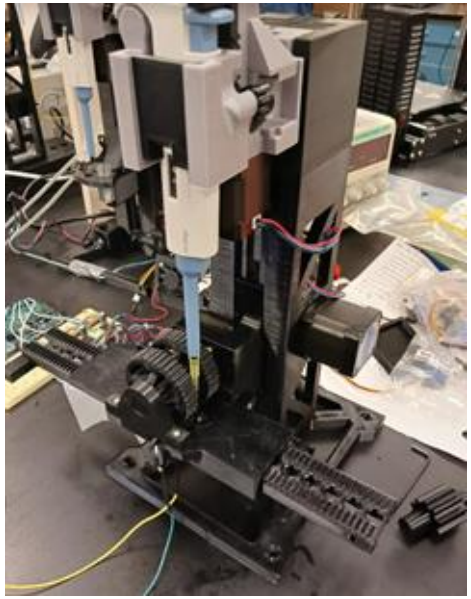
Development of Point of Care Test

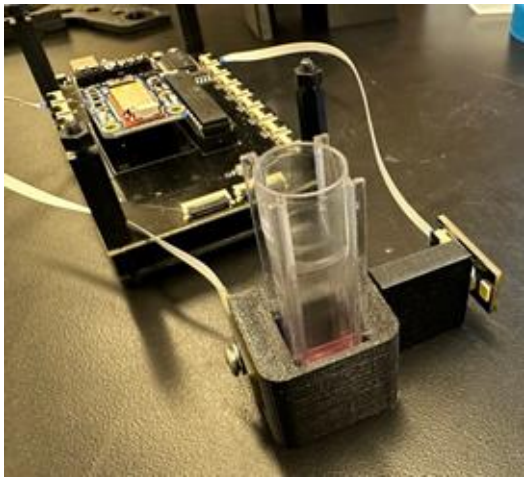
Collect patient urine and clinical information

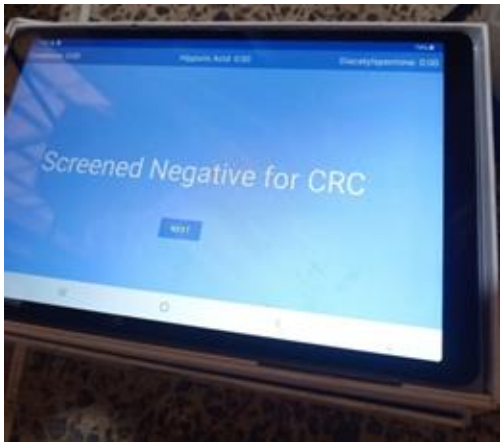
Automatically process urine for metabolite reactions

Automatically run the 3 color reactions and measure the resulting color using the color sensor

Use connected tablet app to calculate metabolite concentrations and combine with clinical data for a final result







75-patient pilot successfully identified CRC patients

- 38 controls; 37 CRC patients
- Sensitivity 95%; specificity 50%

Urine test was easy to use by patients

- 99% no concerns about giving urine sample
- 90% no barriers for participating in CRC screening with urine test
- 99% satisfied
- 77% willing to pay up to $5 for the test

Lessons learned

- Technology gets funded
- Challenging to work on projects where you don’t control large component of it
- Clinician role is to be a technology skeptic

Approaches for screening for CRC in Nigeria

	Average risk	First degree relatives	Symptomatic
FIT	X	X	
Clinical screen			X
Urine metabolites		X	X
Blood methylation panel		X	X

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Breast Cancer early diagnosis

- Widespread population-based breast cancer screening of asymptomatic, average-risk women may not be feasible due to personnel and infrastructural challenges
  - Mean tumor size at presentation to OAU is 10.5 cm

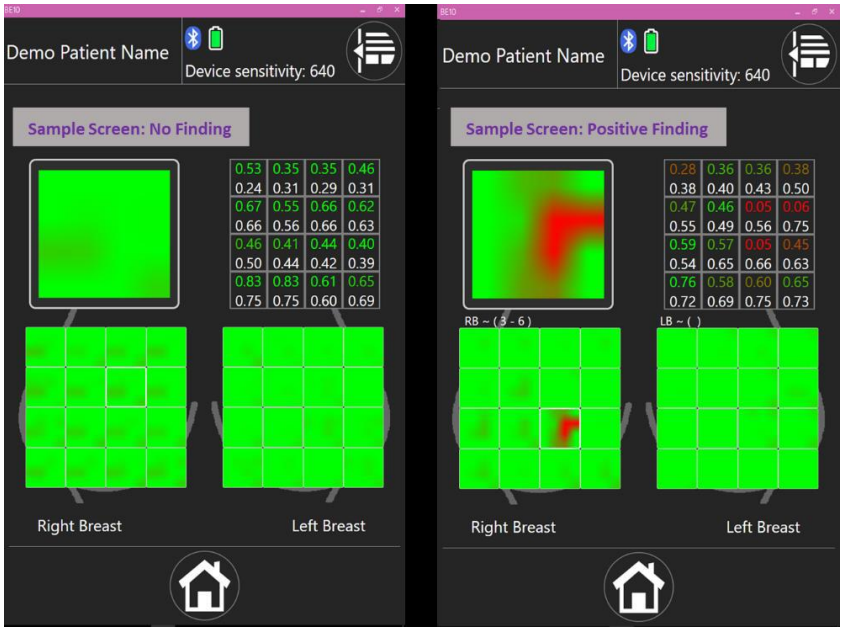


- Nigeria: Limited radiology resources
  - ~300 radiologists in the country (MSK ~150)
  - one per ~500,000 people (US has 50x that)

Delbeke, D and Segall GM. Status and trends in Nuclear Medicine in the United States http://jnm.snmjournals.org/content/52/Supplement_2/24S.full.
Adesunkanmi AR, et al. Breast 2006;15(3):399-409.
Olasehinde O, et al. Int J Cancer 2021;148:2906-14.
RAD-AID Nigeria Country Report. https://www.rad-aid.org/resource-center/country-reports

The iBreastExam versus clinical breast examination for breast evaluation in high risk and symptomatic Nigerian women: a prospective study





prevent cancer FOUNDATION

Mango VL, … Kingham TP. Lancet Global Health. 10(4):555-563.2022

Improving detection of early-stage breast cancer



- Prospective study
- 424 Nigerian women 40 years or older
  - Breast symptoms or
  - Asymptomatic high risk (first-degree relative w/breast cancer)
- Breast cancer education & underwent 4 exams:
  - Clinical Breast Exam (CBE) – experienced surgeon
  - iBE - recent nursing school graduate
  - Mammography
  - Ultrasound

Inexperienced nurse iBE and experienced surgeon CBE similar sensitivity

- Breast level analysis
- Any *SUSPICIOUS* finding

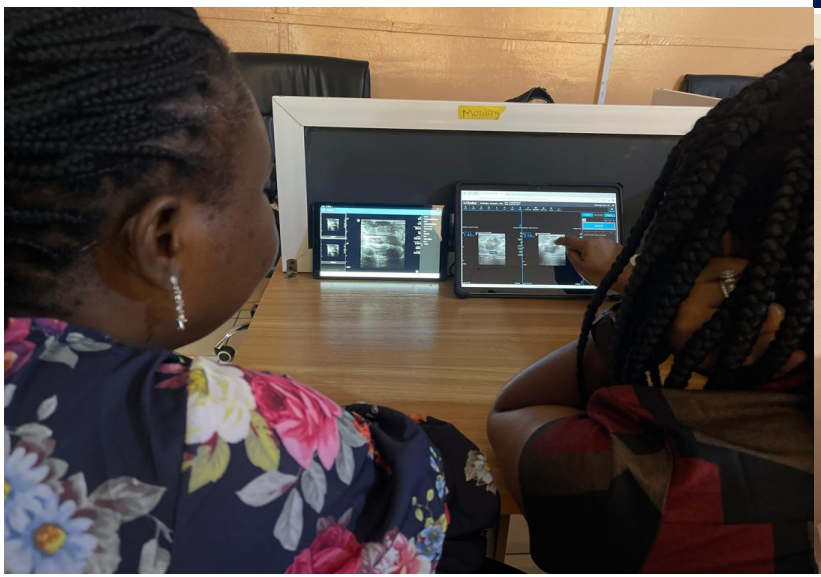
	Sensitivity	Specificity	PPV	NPV
CBE	83%	86%	37%	98%
iBE	86%	50%	14%	98%

- CBE demonstrates better specificity
- Similar NPV
- 13/15 cancers identified by both

Breast Ultrasound AI in Nigeria

- AI education
- Prospective study of women BI-RADS 4 or 5
- Qualitative assessment of radiologists AI experience

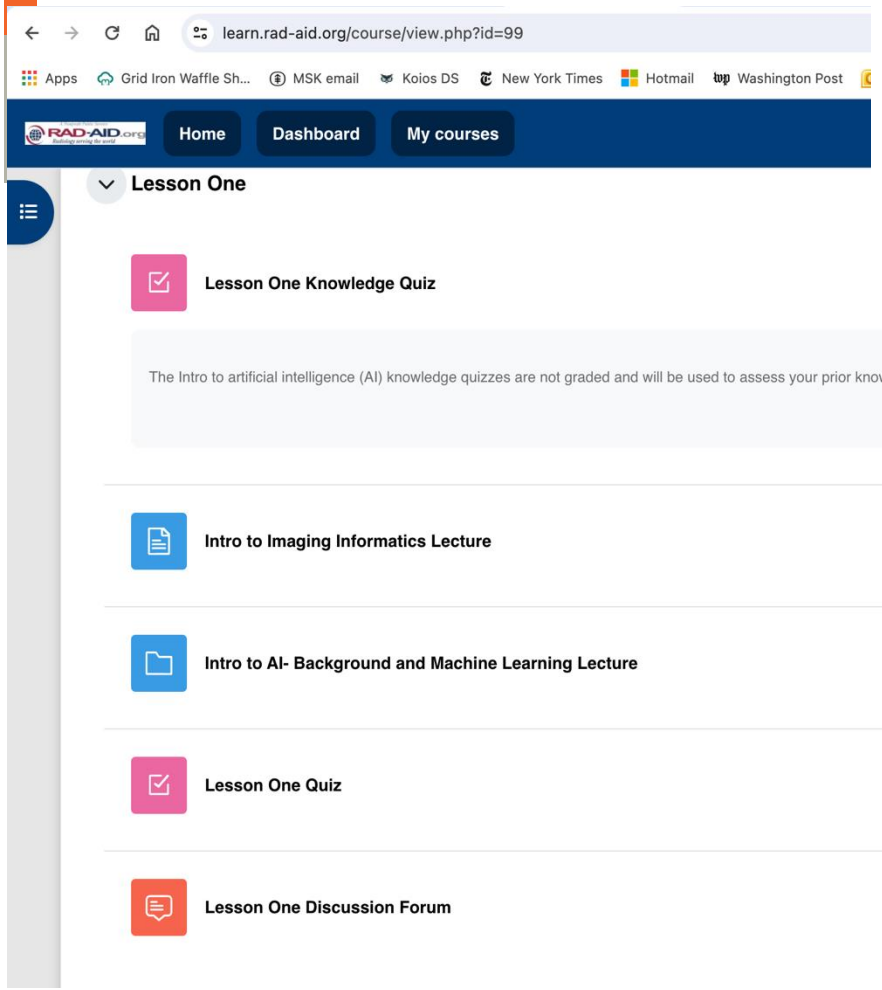






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RAD-AID.org

Radiology serving the world





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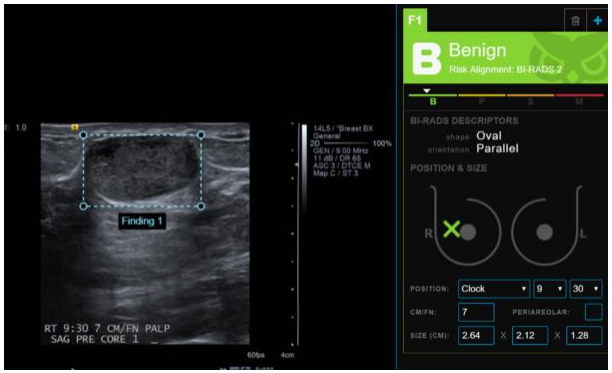
Artificial Intelligence Decision Support for Timely Breast Cancer Diagnosis in Nigeria

African Research Group for Oncology

Memorial Sloan Kettering Cancer Center

Goals/Aims:

1.Train 4 radiologists from two institutions in Nigeria to utilize a tablet-based AI decision support system and interpret AI outputs on breast ultrasound images acquired on tablet-based ultrasound



2. Test the accuracy of tablet-based breast ultrasound AI decision support (Koios DS Breast) in a multi-center LMIC setting

3. Assess the experiences and opinions of the 4 Nigerian radiologists in using breast ultrasound AI decision support

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Breast US AI: Results

- 155 Nigerian women w/ 184 BI-RADS 4 or 5 masses (51 benign/133 cancers)

- Tablet US images successfully underwent AI analysis by Nigerian radiologists

- AI analysis:
  - 166 masses positive (probably malignant or suspicious AI output)
  - 18 masses negative (benign or probably benign AI output)

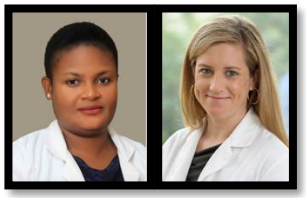
- AI correlated with pathology results:
  - Sensitivity 95% (127/133)
  - Specificity of 24% (12/51)
  - PPV 77% (127/166)
  - NPV 66% (12/18)

Mobile ultrasound overcomes many barriers to patient early diagnosis

- AIM 1: Develop a competency-based mHealth US-guided breast biopsy-training program for LMIC radiologists and validate the assessment metrics.

- AIM 2: Train ten ARGO Nigerian radiologists to perform US-guided breast biopsies using the competency-based mHealth training program.





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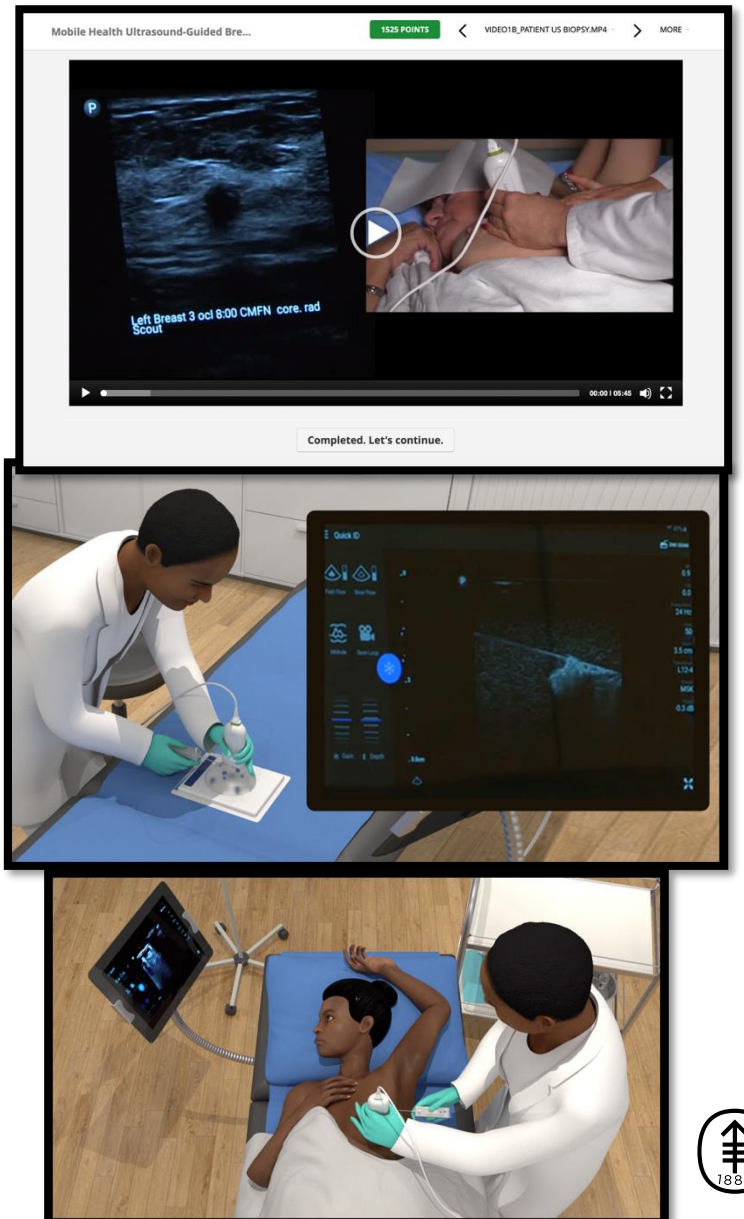
Supported by R21 CA239784-01 (PIs: Sutton, Omisore)

AIM 1: mHealth US-guided breast biopsy competency-based training program

Blended Learning

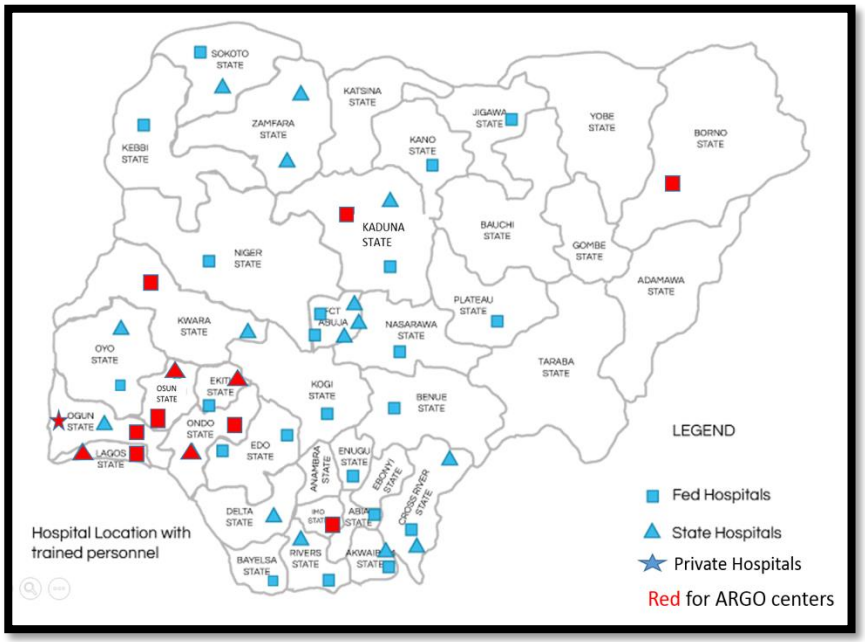
Simulation Biopsy

Patient Biopsy



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AIM 2: Train thirteen Nigerian radiologists to perform and clinically implement US-guided breast biopsies





Median time from first medical presentation to surgical consultation was **41 days** (IQR 23, 89), which is below the WHO target of 60 days for breast cancer early diagnosis

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30% increase in population-level access to breast cancer early diagnosis

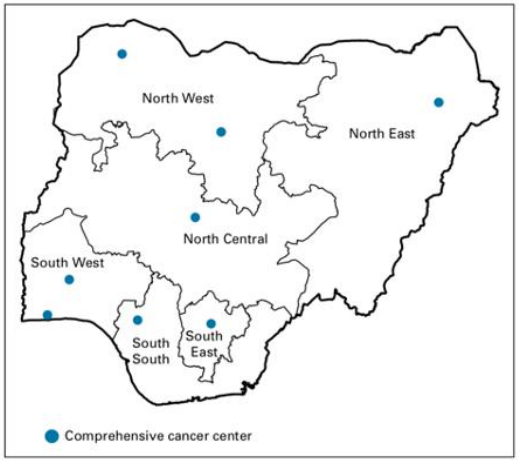
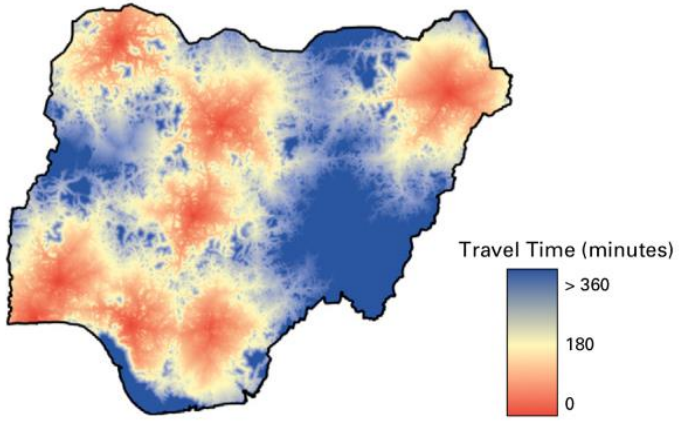
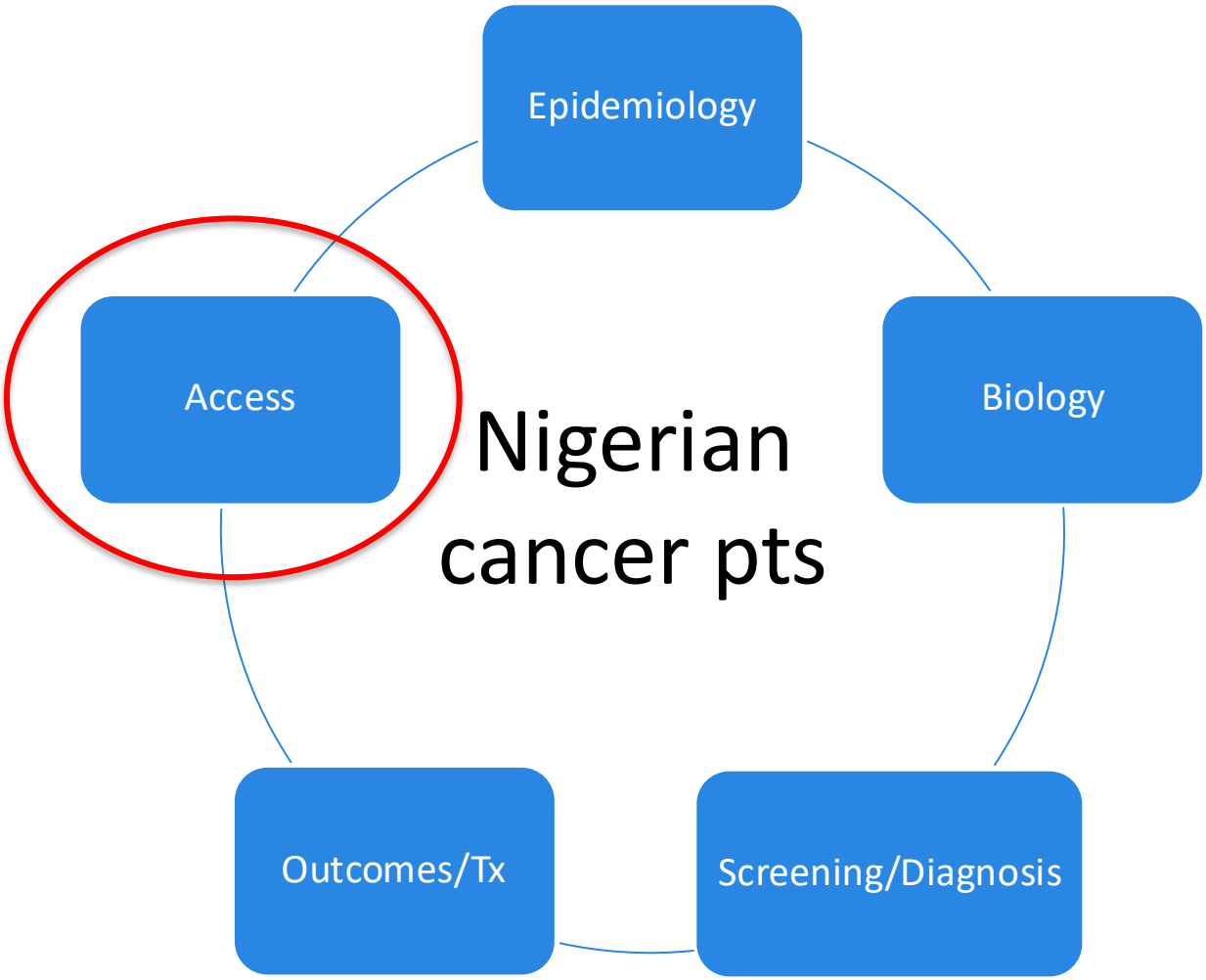


FIG 1. The geopolitical zones of Nigeria and the comprehensive cancer centers.



Knapp GC et al. Manuscript preparation.

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Epidemiology
Biology
Screening/Diagnosis
Outcomes/Tx
Access
Nigerian cancer pts

Access and barriers to care in Nigeria

- Financial catastrophe
  - 10% or 25% of annual salary
  - 22 women after breast cancer dx
  - 75-95% of patients experienced financial catastrophe
  - 27% altered treatment due to finances

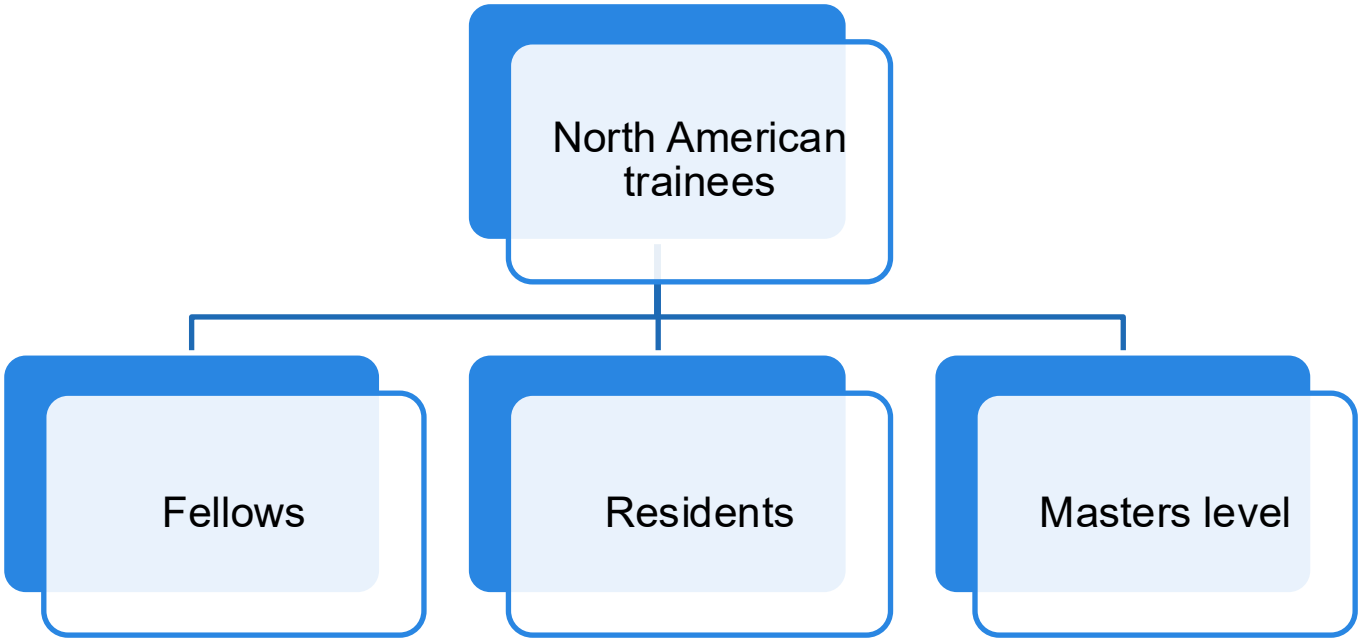
- Primary barrier to oncology care
  - Juliet Lumati, MD initiating intervention study 2024

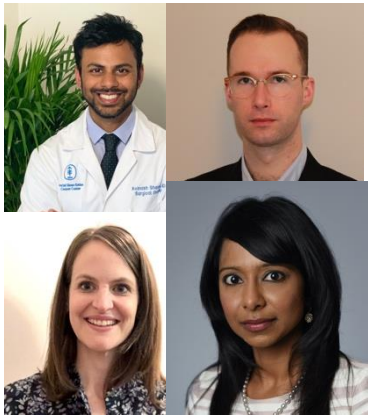
Wuraolo, …, Knapp Journal of Cancer Policy, 42, 2024

GCDI Training: Nigerian trainees

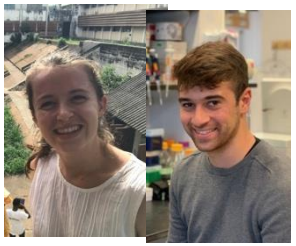


GCDI Training: North American trainees









Cancer care is a global priority

- We cannot understand cancer biology/treatments/culture without studying it globally
- Cost-effective cancer research
- Focus on workforce and research is needed to improve outcomes
- Global collaborations with leadership from LMICs required to generate regional data to guide care
  - Don’t extrapolate high-income country data to LMICs!!

Global Cancer Disparity Initiative Support

- MSK Physician in Chiefs Office
- MSK International Center
- Thompson Family Foundation
- NCI:
  - R01 Modifiable risk factors for colorectal cancer in Nigeria
  - R01 Developing a blood-based point-of-care CRC diagnostic test
  - UG3/UH3 Point-of-Care Cancer Screening Test
  - R21 m-Health Cancer Screening in LMIC
  - NCI Center for Global Health Pilot
  - CRDF Research Capacity Building Grant
  - D43 Building the Nigerian Cancer Research Training Program
  - P20 An Immuno-oncology center in Nigeria
- Prevent Cancer Foundation
- Oak Foundation
- MSK Population Science Award

Thank you!



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