Esophageal Cancer in Tanzania

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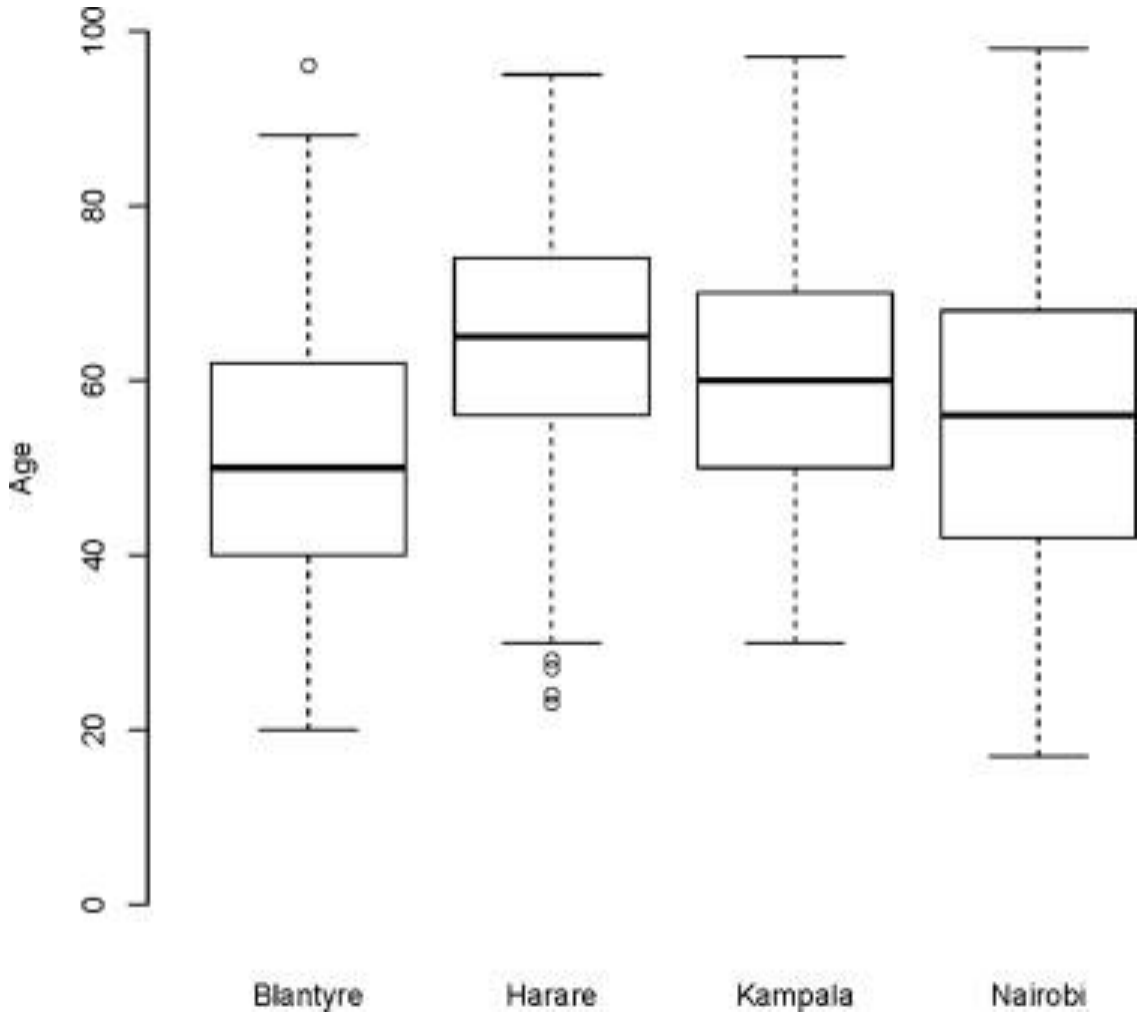


Fig. 1. Age distribution for cases of oesophageal cancer, for four population-based cancer registries in Eastern Africa, 2004–2008.

Cheng, M. et al. The incidence of oesophageal cancer in Eastern Africa: Identification of a new geographic hot spot? *Cancer Epidemiology. 2015. 39(2): 143-9.* http://dx.doi.org/10.1016/j.canep.2015.01.001

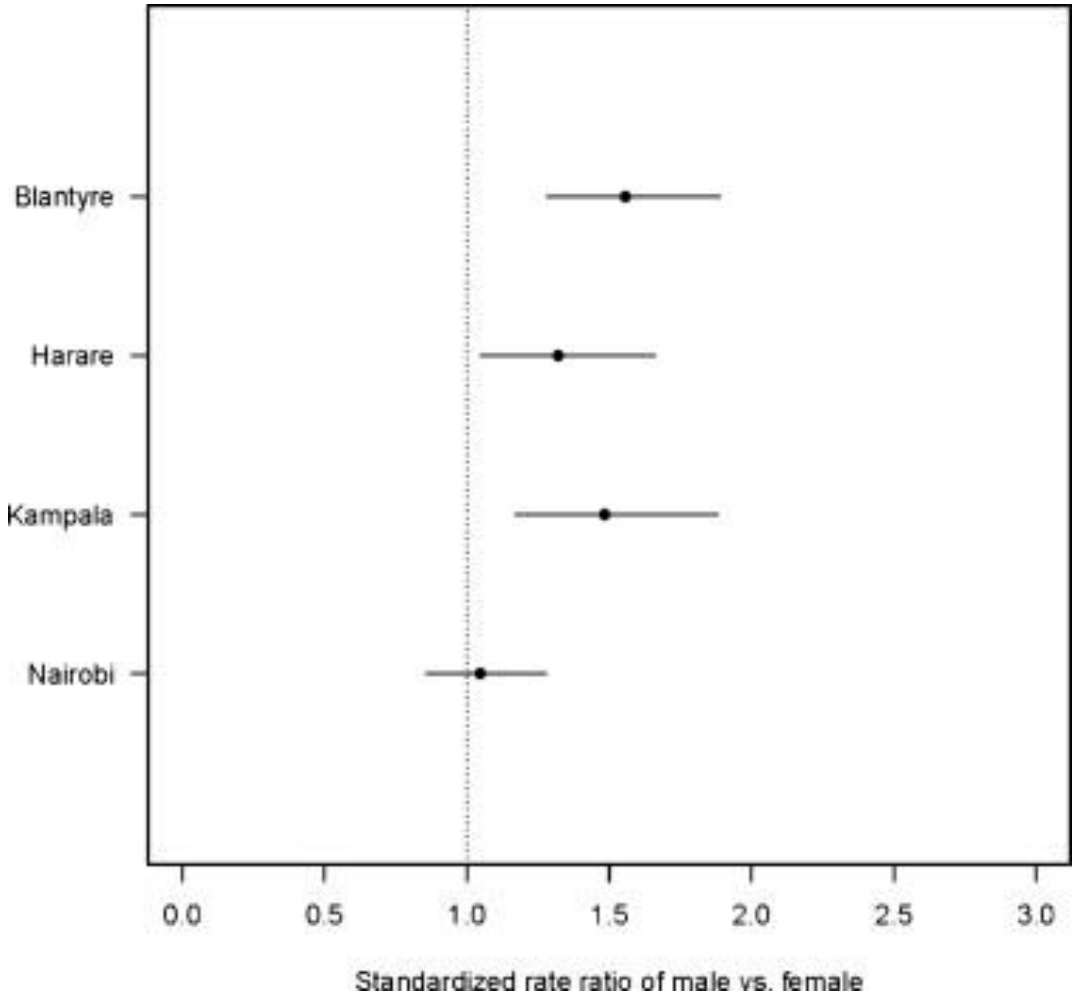


Fig. 2. Standardized rate ratios (SRRs) for oesophageal cancer in males versus females in four urban populations in Eastern Africa, 2004–2008.

Cheng, M. et al. The incidence of oesophageal cancer in Eastern Africa: Identification of a new geographic hot spot? *Cancer Epidemiology. 2015. 39(2): 143-9.* http://dx.doi.org/10.1016/j.canep.2015.01.001

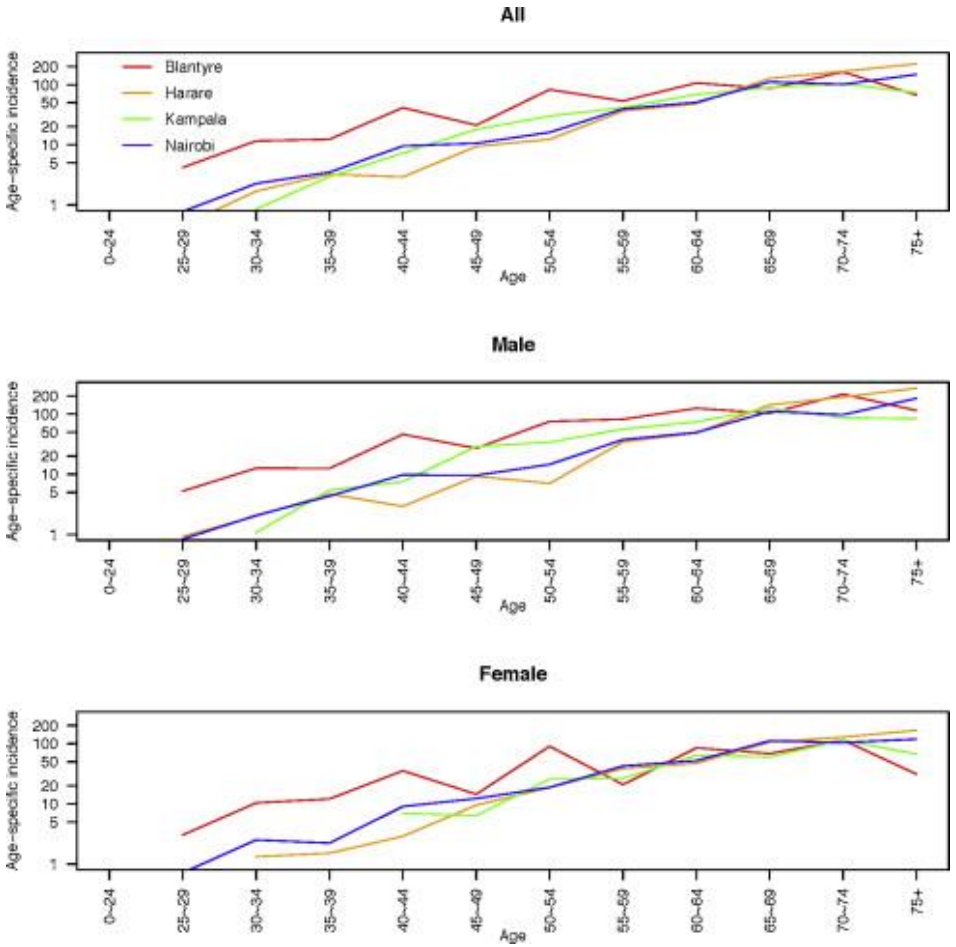


Fig. 3. Age-specific incidence rates for oesophageal cancer for four population-based cancer registries in Eastern Africa, 2004–2008.

Cheng, M. et al. The incidence of oesophageal cancer in Eastern Africa: Identification of a new geographic hot spot? *Cancer Epidemiology. 2015. 39(2): 143-9.* http://dx.doi.org/10.1016/j.canep.2015.01.001

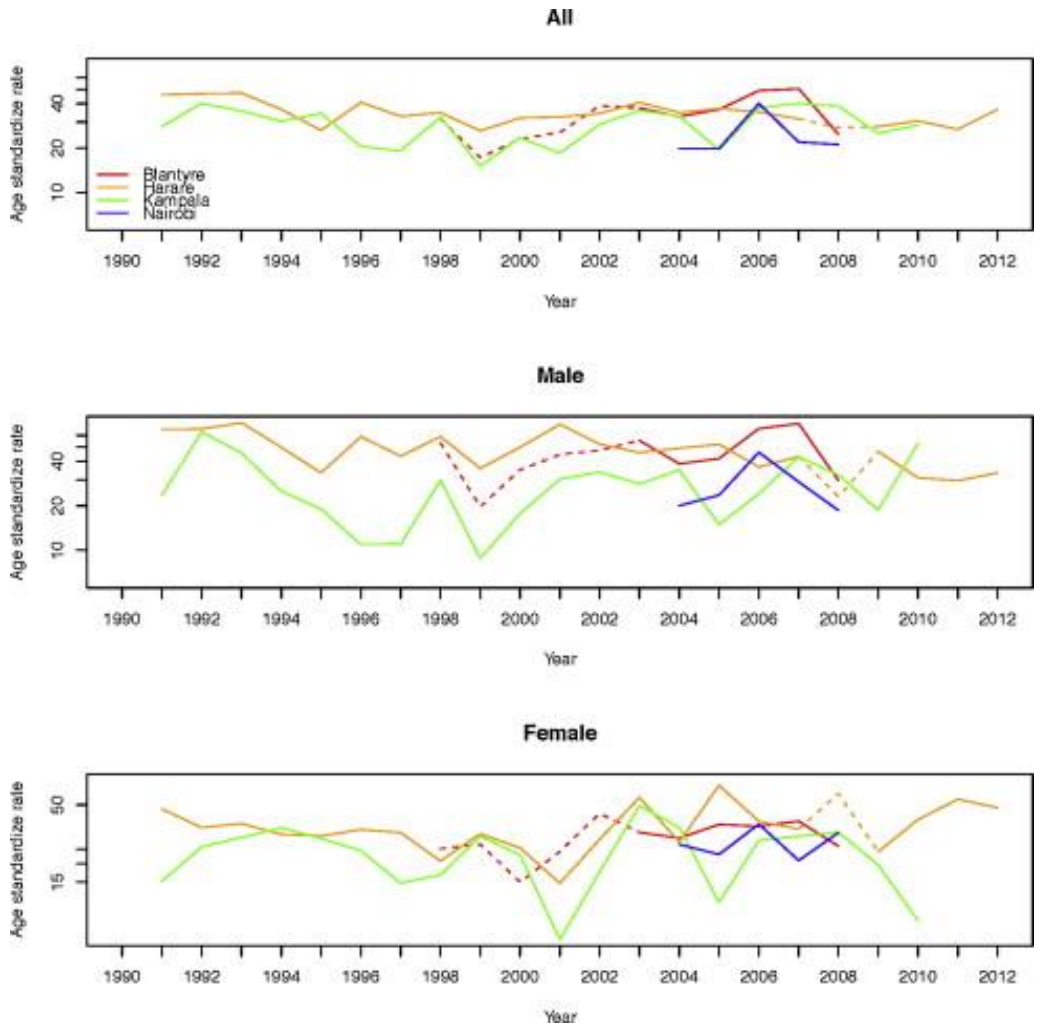


Fig. 4. Trends in ASRs for oesophageal cancer over time from four population-based cancer registries in Eastern Africa, 1990–2012.

Cheng, M. et al. The incidence of oesophageal cancer in Eastern Africa: Identification of a new geographic hot spot? *Cancer Epidemiology. 2015. 39(2): 143-9.* http://dx.doi.org/10.1016/j.canep.2015.01.001

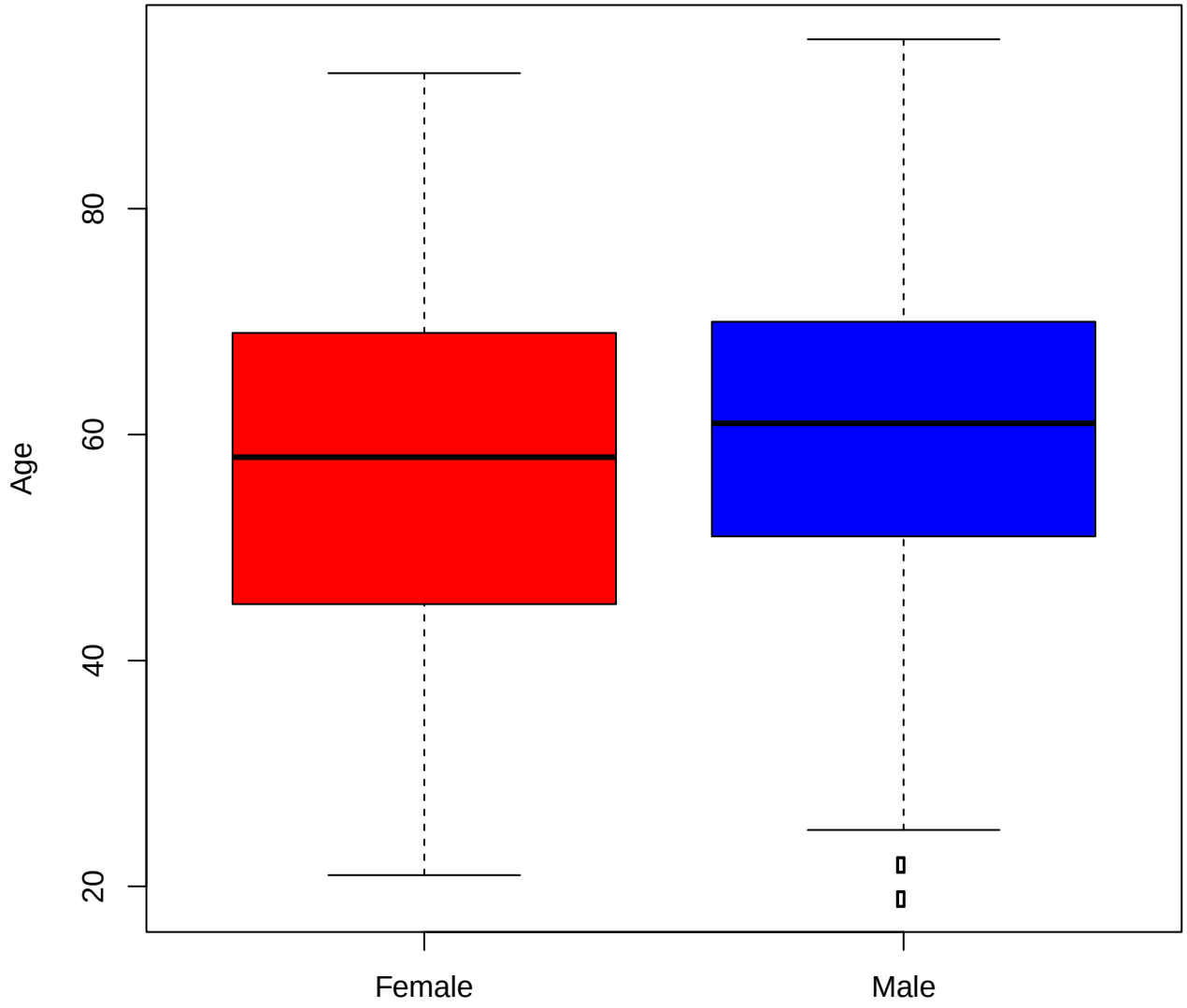


Figure 1. Age distribution at time of diagnosis, according to gender.

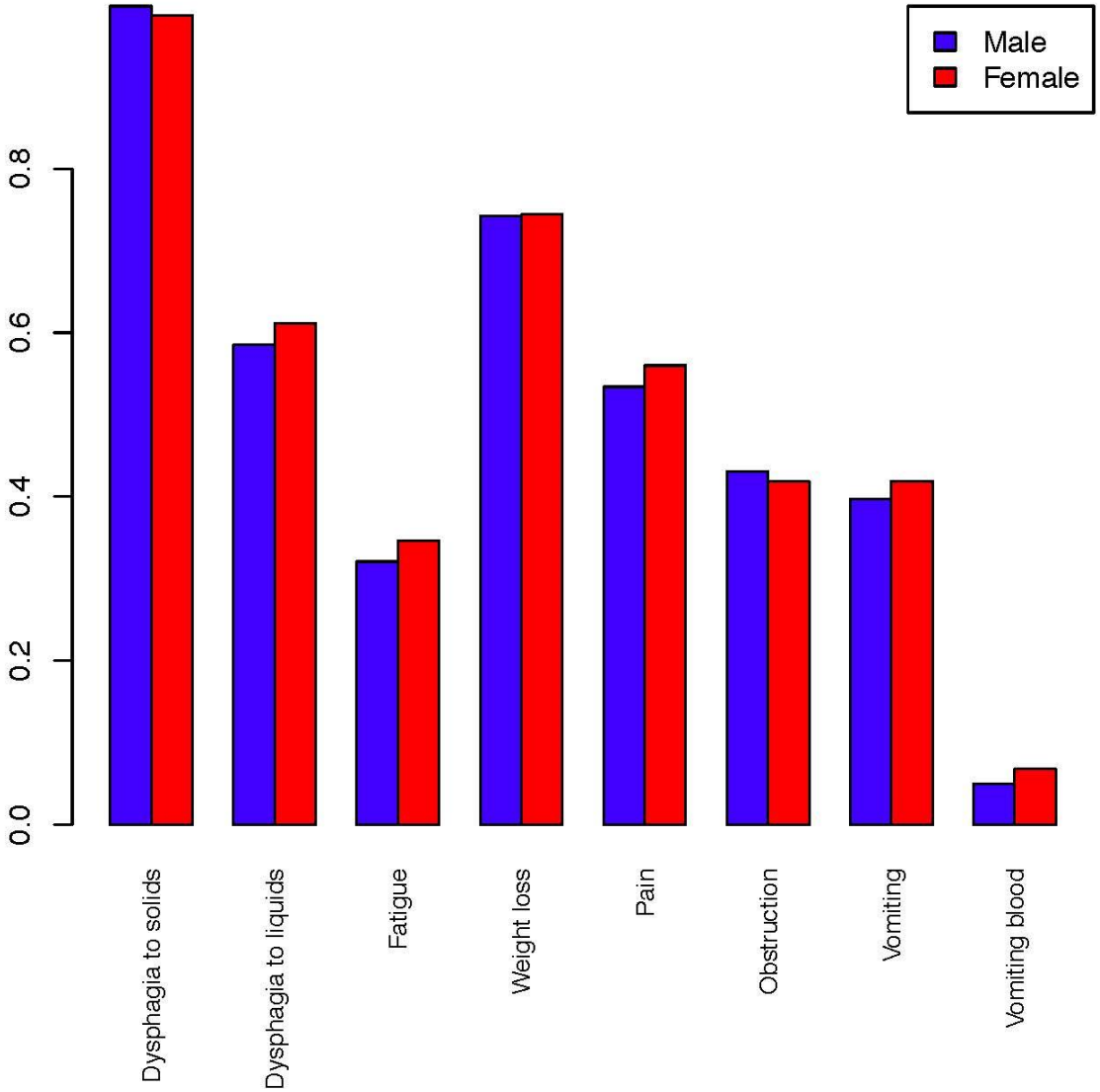


Figure 2. Documented symptoms at presentation.

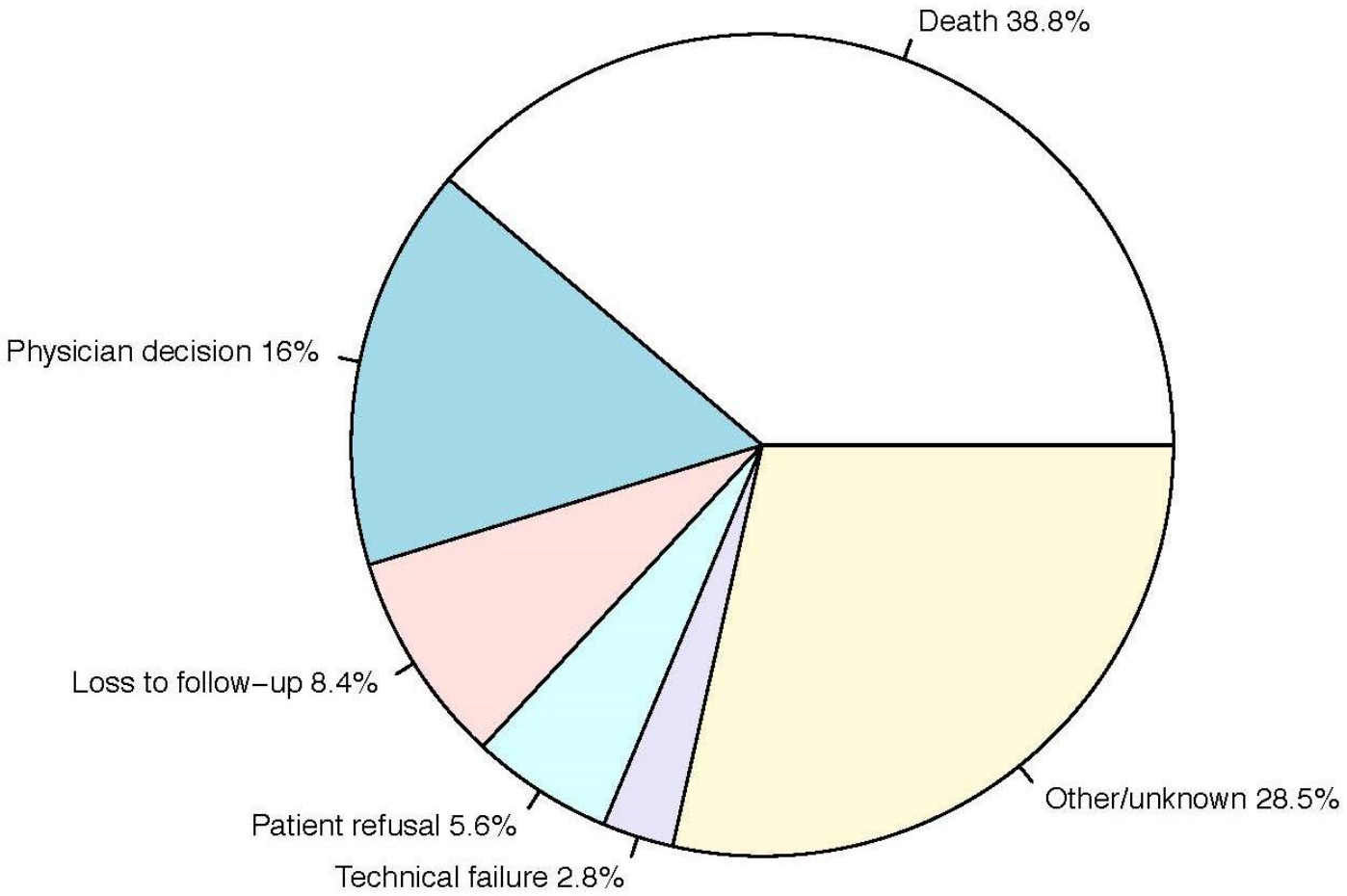


Figure 3. Documented reasons for early discontinuation of treatment.

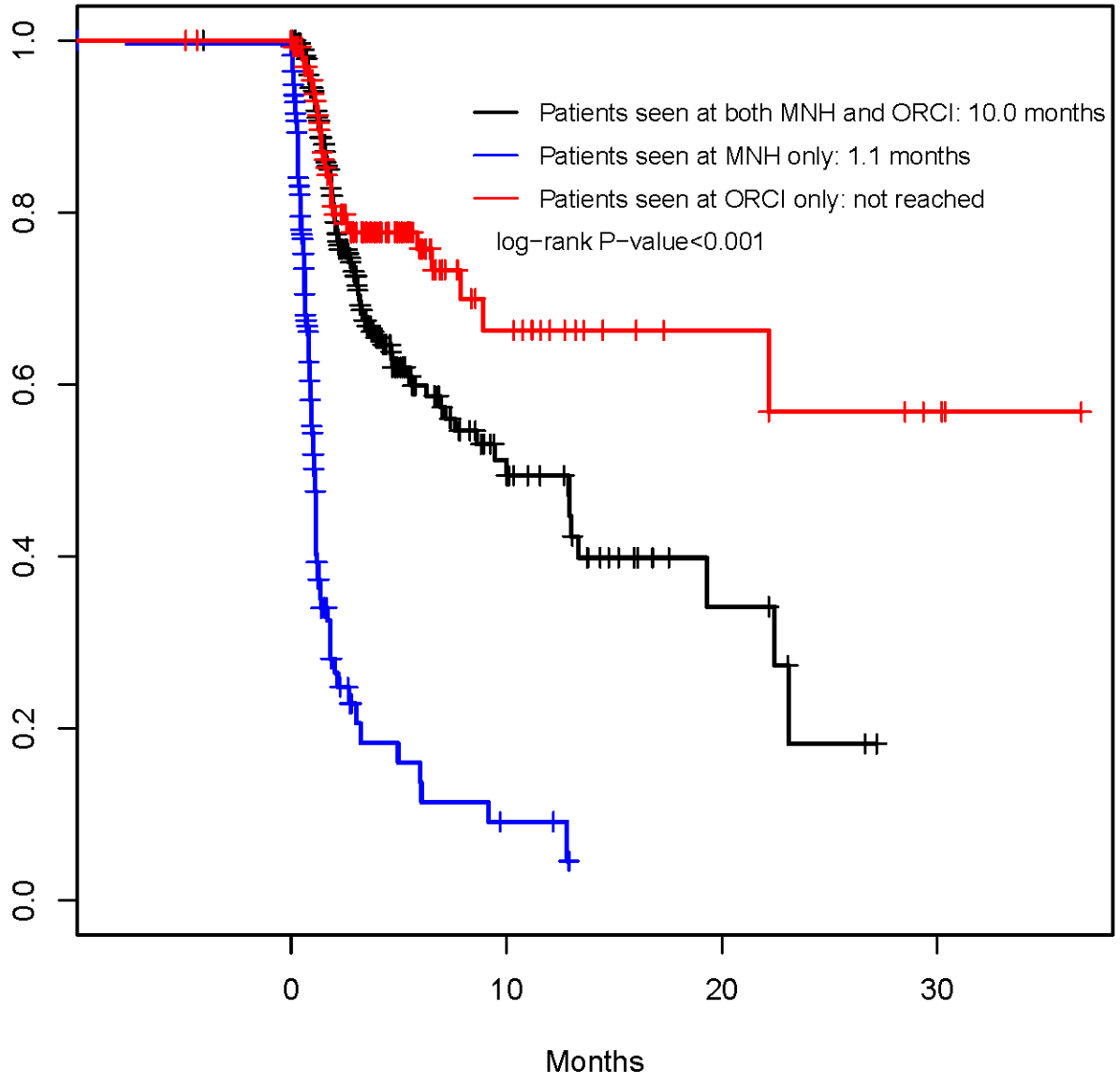


Figure 4. Overall survival according to site(s) where patients received care.

Case-Control Study

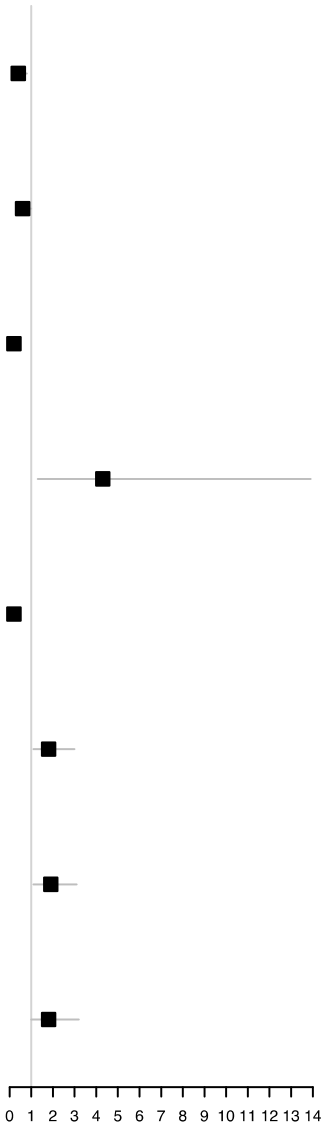
- Study Aim: To evaluate potential etiologic effects of dietary, lifestyle behaviors, and environmental factors contributing to the high-incidence of EC in Tanzania.

Case-Control Study: Methods

- Cases were recruited from patients with newly diagnosed EC receiving care at either Muhimbili National Hospital (MNH) or Ocean Road cancer Institute (ORCI) in Dar es Salaam.
  - Age ≥30 years
  - Diagnosis based upon either histopathologic confirmation or clinical suspicion (e.g., barium swallow)
- Controls recruited 1:1 from hospitalized patients at MNH
  - Only with non-malignant conditions
  - Matched by gender and age (±10 years)
- E*nvironmental*, *dietary*, and *lifestyle* exposures were collected through face-to-face quantitative interviews with both cases and controls.
  - A surrogate (close family member) was interviewed in the event a case was unable to participate in an hour-long interview.
  - All interviews were performed in Swahili by two trained Tanzanian researchers.
- All cases and controls were asked to provide a saliva specimen for DNA collection.

Case-Control Study: Results of multivariate analysis*

	OR	LCI	UCI
Eat fruit daily	0.4	0.2	0.8
History of anemia	0.6	0.3	1
Reguarly use medication	0.2	0.1	0.3
Family history of esophageal cancer	4.3	1.3	13.9
Lives in household with TV	0.2	0.1	0.4
Lives in household with running water	1.8	1.1	3
Annual household income<1.2M TZS	1.9	1.1	3.1
Current/former smokers	1.8	1	3.2

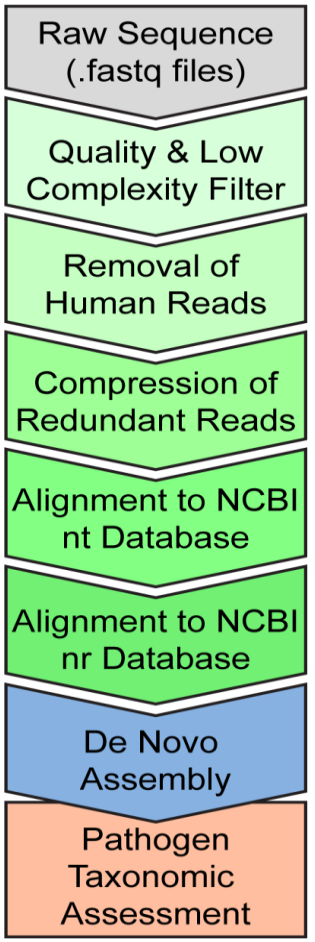


*** all factors with p-value <0.2 in univariate analysis**

Our Current Study:
Molecular Determinants of Esophageal Cancer

- Primary Aims:
  - To determine the transcriptome of Tanzania EC tumor specimens for pathogen-encoded RNA.
  - To evaluate the somatic mutational rate, mutational pattern, copy number profiles, and recurrently mutated genes in tumor specimens obtained from EC patients in Tanzania.

- Secondary Aim:
  - To determine a system that is cost-effective, easily transportable, and preserves genetic integrity and expression profiles of samples, breaking down barriers for sample acquisition and subsequent analyses of DNA *and* RNA.



Pathogen identification pipeline

Systems of Comparison:

Fixative Methods

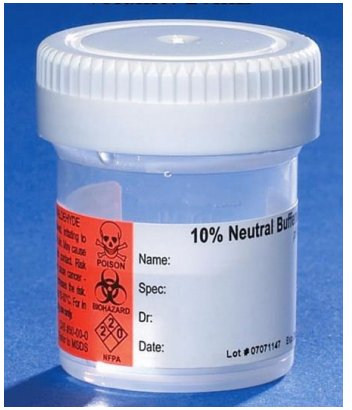
PAX

- "Preserves histomorphology and biomolecules for purification of high-quality RNA, DNA, miRNA, proteins, and phosphoproteins from a single sample."

RNALater

- "Nontoxic tissue storage reagent that rapidly permeates tissue to stabilize and protect RNA"
- Histology shown to give excellent morphological detail when examined for standard histological criteria

Formalin



- Toxic
- Good for immunohistochemical techniques
- Bad for Extraction of high quality nucleic acid

Tissue Preparation Workflow

1. Sample acquisition

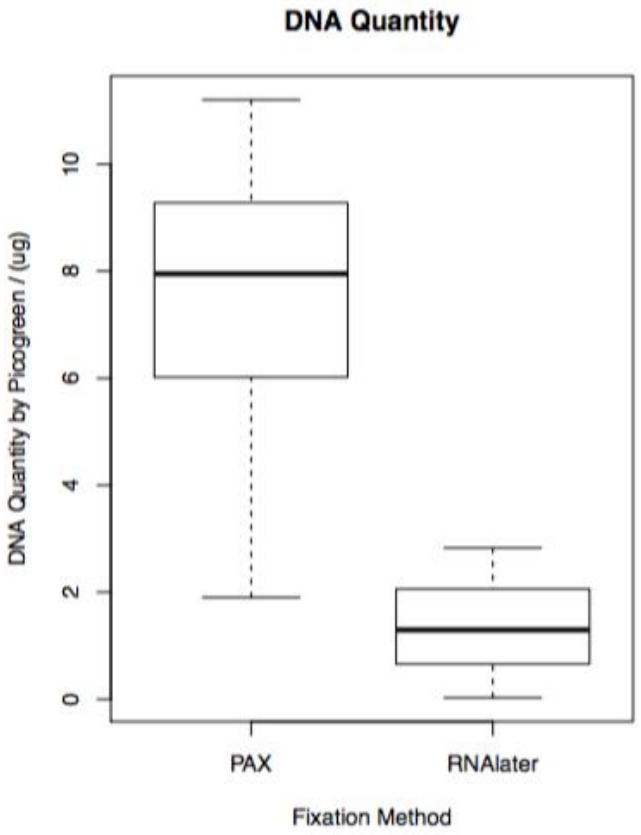
2. Fixation/Stabilization

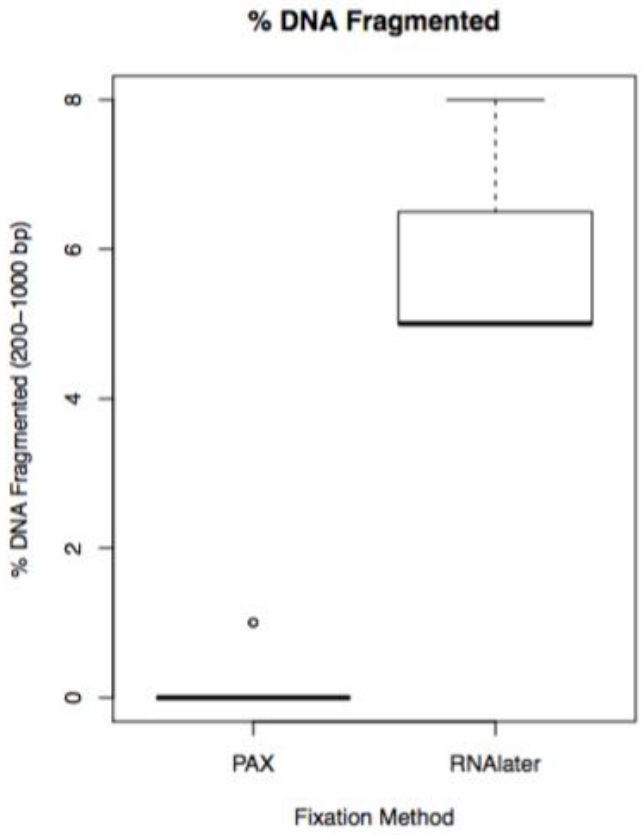
3. Refrigeration

4. Shipment

5. Storage

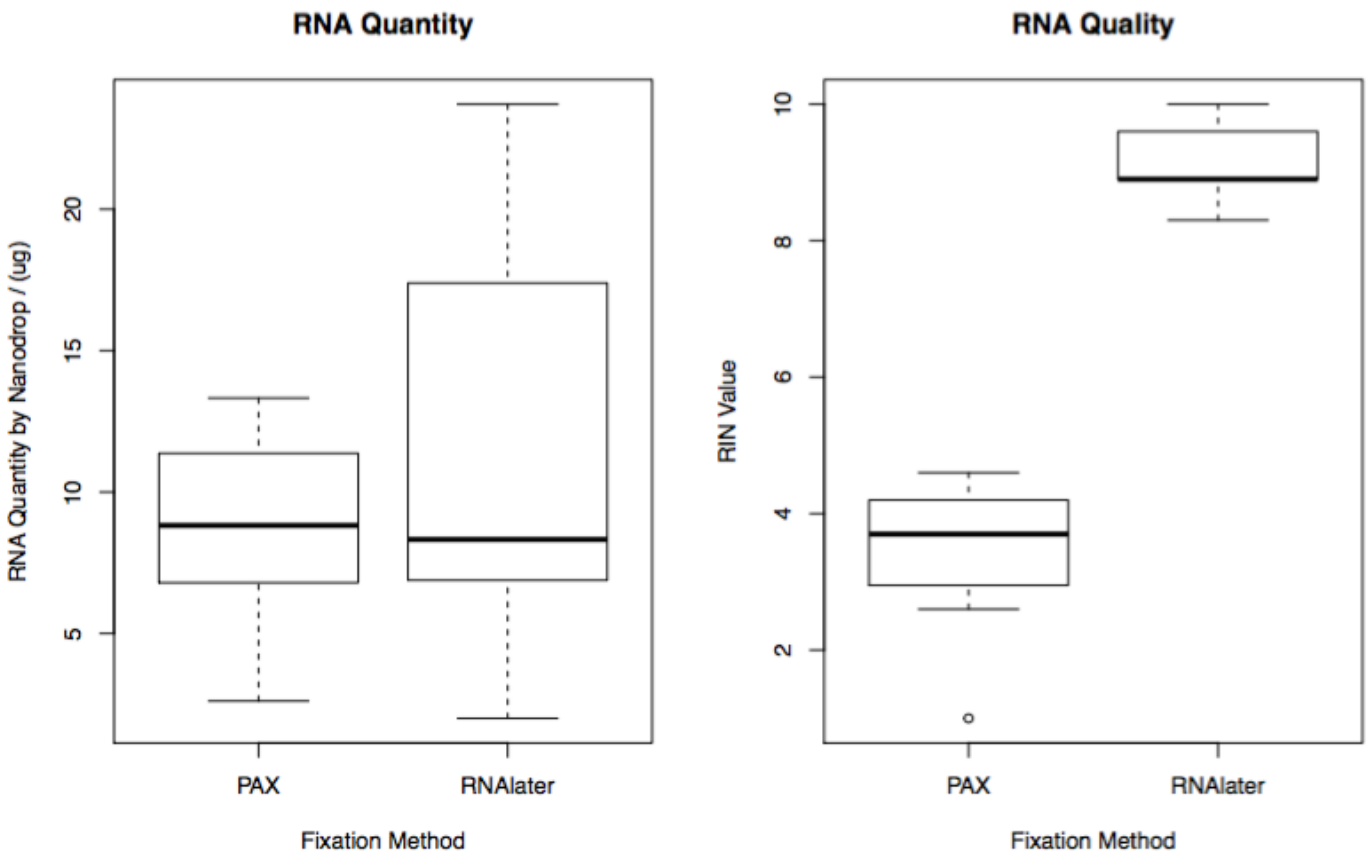
DNA Analysis





- DNA quantity: PAX > RNAlater
- DNA quality: PAX > RNAlater

RNA Analysis

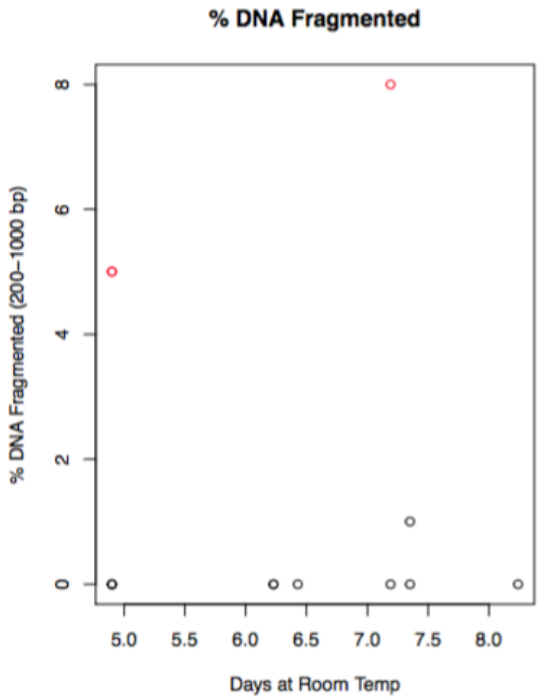


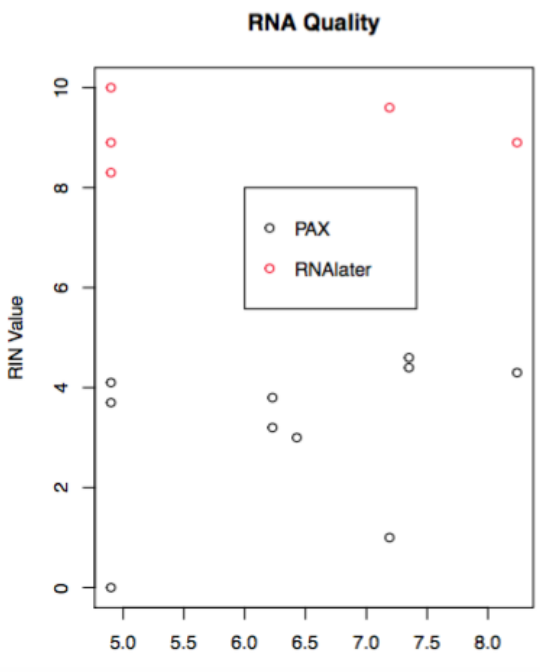
- RNA quantity: PAX = RNAlater(similar in quant)
- DNA quality: PAX < RNAlater*(sign. better)

Travel Analysis:
Does travel time effect quality of DNA/RNA?

- DNA/RNA quality seems to not be impacted by length of time outside of 4 degree, up to 9 days (our max)

- PAX and RNAlater prove to be flexible and ideal for field collection





Summary of Pilot Study of Molecular Analyses

- PAX:
  - DNA and RNA quantity very high
  - DNA quality extremely good
  - RNA quality not great, RIN <= 4

- RNAlater:
  - DNA quantity low (*possible that our extraction protocol can be improved in subsequent samples)
  - DNA quality good, but less so than PAX
  - RNA quantity comparable to PAX
  - RNA quality extremely good, RIN ~ 9

Difficult Questions and Challenges

- Even within Africa, this is likely a heterogeneous disease within geographic sub-populations
  - Need for a multi-site African GWAS with coordinated effort to correlate genetic risk with environmental factors.
  - Comparison of molecular findings across sites.
- Development and sharing of creative, low-cost solutions to study geographically isolated diseases
- Need to explore palliative stenting for esophageal obstruction
  - Sustainable stent availability, not just for research
  - Scalability: need for centralized training for endoscopic techniques
  - Plans to study feasiblity and QOL outcomes

Funding Sources

NIH/NCI P30 Supplement for “Pilot Collaborations with LMICs in Global Cancer Research” [Contract No. HH5N261200800001E].

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