African ESCC Case-Control Consortium

- Why?

  No suitable cohorts
  Primary prevention
  Power
  Risk stratification for screening

- Priority risk factors to investigate
- Current fieldwork

Research Perspective

- Encompass a broad range of putative risk factors

- Priority factors for investigation are those established or probable carcinogens in other settings
  - Identify exposure sources
  - Evaluate as risk factors and their contribution to African EC burden

- Undertake research in multiple settings
  - interpret findings both locally and in terms of the African EC corridor
  - Co-ordinate harmonized effort, for pooling
  - Include tumor and biospecimen

Previous Studies

Country, location[a]	Recruitment	No. cases : controls	Tobacco	Alcohol	HAP	HIV	Other findings
S. Africa – Gauteng	1953-55	44 : 44	↑	↑	•	•	↑ in miners
S Africa – Gauteng	1963-?	196 : 1064	↑	↔	•	•	
Zimbabwe	1963-77	881: 5238	↑	↔	•	•	↑ in miners
S. Africa – KZN	1978-81	211 :211	↑	↑		•	↑ commercial maize
S. Africa – Gauteng	1984-85	200 : 391	↑	↑	•	•	
S. Africa – E. Cape	1987-88	100 : 100	↑	↔	•	•	↑ solanum nigrum, ↑ trad. Med
S. Africa - Gauteng	1995-99	405 : 2174	↑	↑	•	↔	
S. Africa – KZN	~2000?	87 : 121	↑	↑	↑	•	
S. Africa – E. Cape	2001-03	670 : 1188	↑	↑			↓ green leafy veg ↓ fruit, ↑maize+wild greens+ beans
S. Africa – E. Cape	Not stated	234 : 595	↑	↔	•		No assoc. with iron overload
Kenya, Eldoret	2003-06	159 : 159	↑	↑	↑	↔	↑ hot drinks, ↑ tooth loss (unadj)
Uganda, Kampala	2004-05	55 : 232	↑	↔	•	•	
Malawi	2011-13	96 : 180	↑		↑		↑ white maize flour
Zambia, Lusaka	2013-14	50 : 50	↑	↑	↑	↑	

IJC
International Journal of Cancer

Informing etiologic research priorities for squamous cell esophageal cancer in Africa: A review of setting-specific exposures to known and putative risk factors

V.A. McCormack[1], D. Menya[2], M.O. Munishi[3], C. Dzamalala[4,5], N. Gasmelseed[6,7], M. Leon Roux[1], M. Assefa[8], O. Osano[9], M. Watts[10], A.O. Mwasamwaja[3,11], B.T. Mmbaga[3,11], G. Murphy[12], C.C. Abnet[12], S.M. Dawsey[12] and J. Schüz[1]

- Alcohol
  - Sachets - tujilijili, virobas
  - Local brews – spirits gongo, changaa
- Tobacco
  - Smoking
  - Snuff and chewing, incl. ugoro, betel quid (kuberi) with tobacco
- Hot beverages / porridge / nsima
  - Tongue burning, beverage type
- PAH: Indoor pollution, mursik, dukhan, charcoal

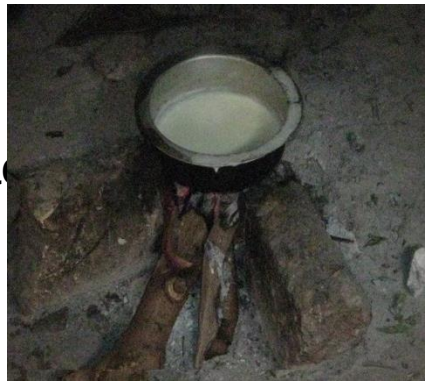
Priority risk factors to study

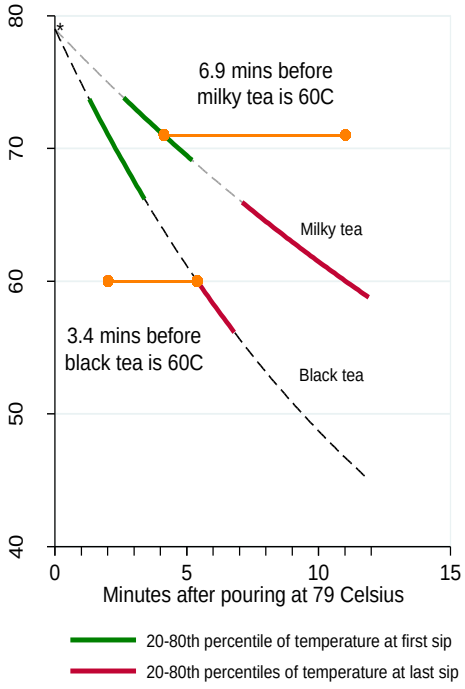
- Low intake of fresh fruits and vegetables, nutrient deficiencies
- N-nitroso compounds: water sources, nitrates in food
- Oral health
  - Fluorosis index, DFMT score, leukoplakia, method of tooth brushing: toothbrush, wood, mkaa
- Animal contact
- Ptaquiloside –from pteridium aquilinum – bracken?
- Mycotoxins?
- Geophagia

Munishi et al, 2015. Cancer Causes & Control

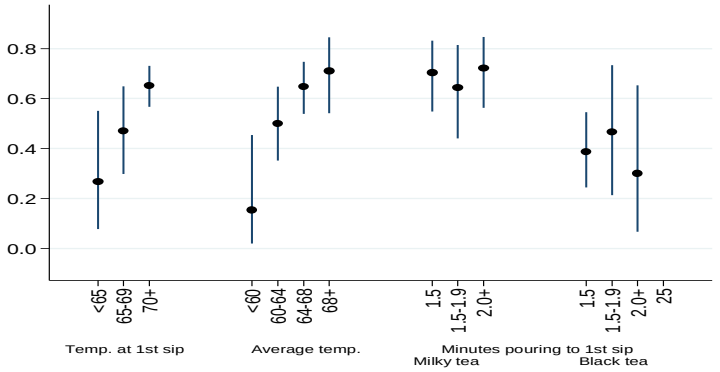
Raw data – temperatures at first and last sip for milky and bla

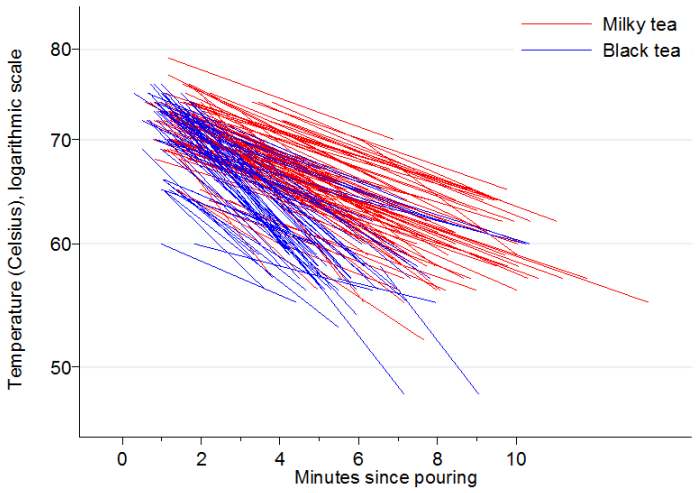
- Black tea cools faster
- Black tea is sipped faster
- Milky tea is hotter throughout, despite waiting longer





*Medium temperature at pouring, 79 Celsius. Cooling curve for ambient temperature of 20C





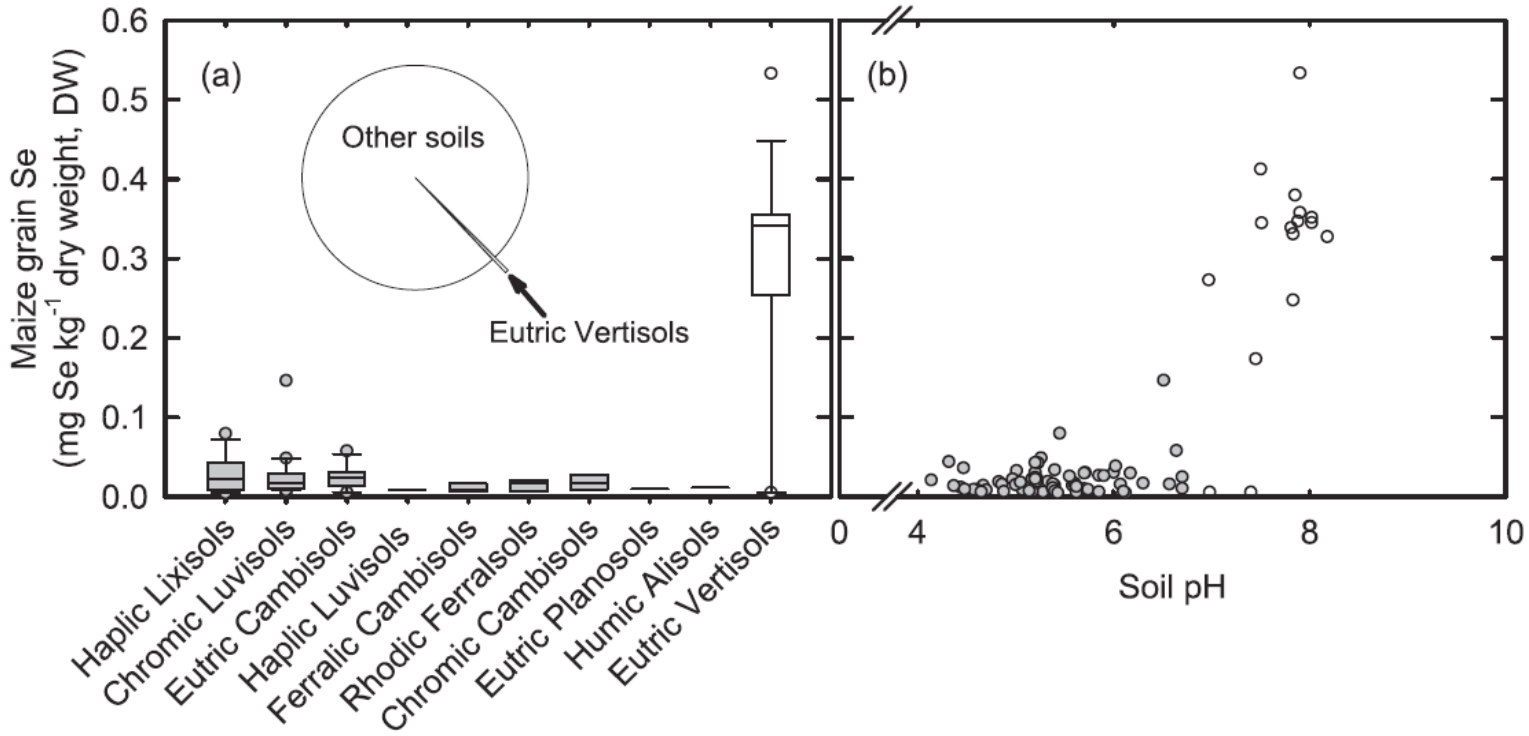
International Agency for Research on Cancer

World Health Organization

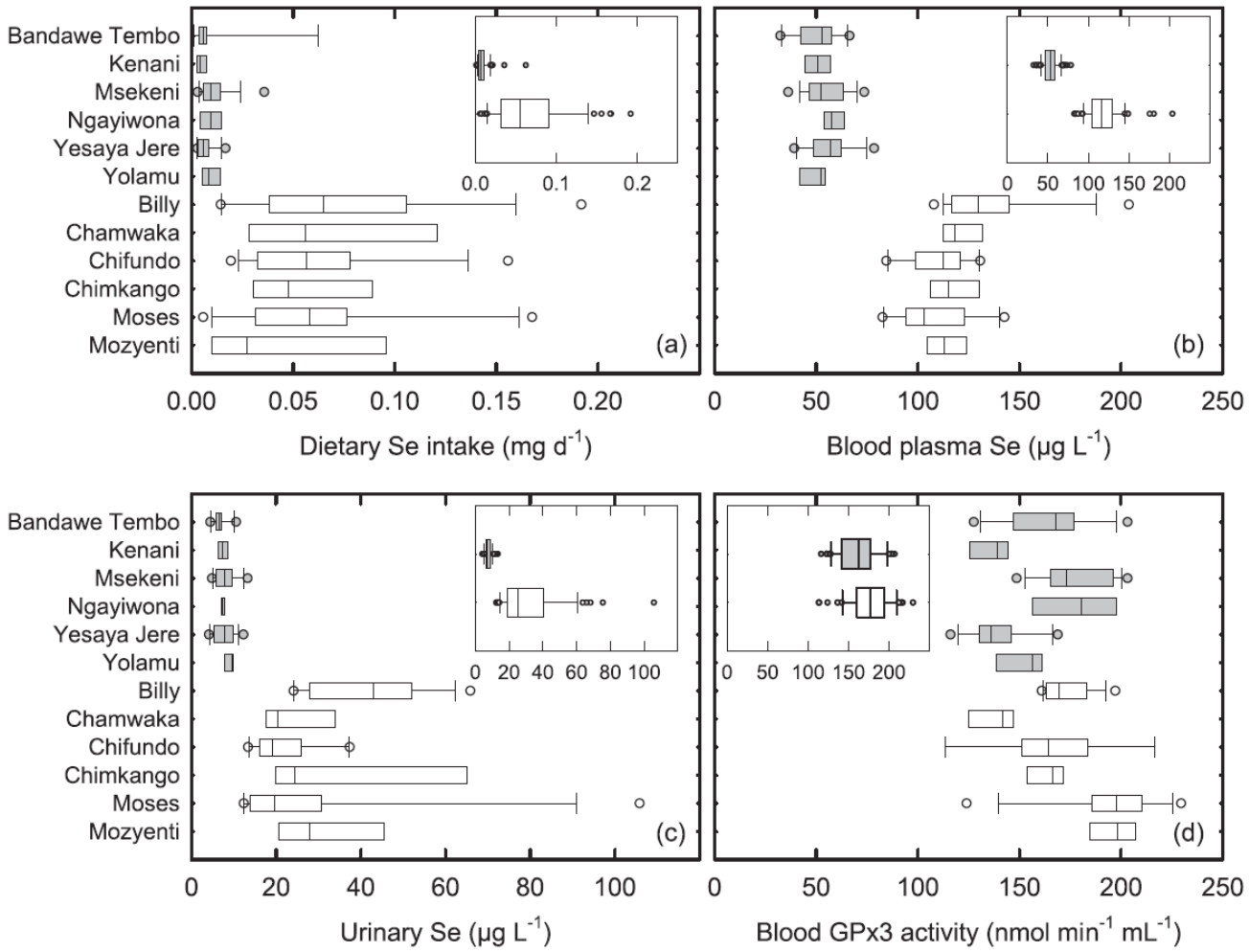
Suggestions of Micronutrient deficiencies

40% Se deficiency in Malawi, under by geochemical control

Restricted locally-sourced diet

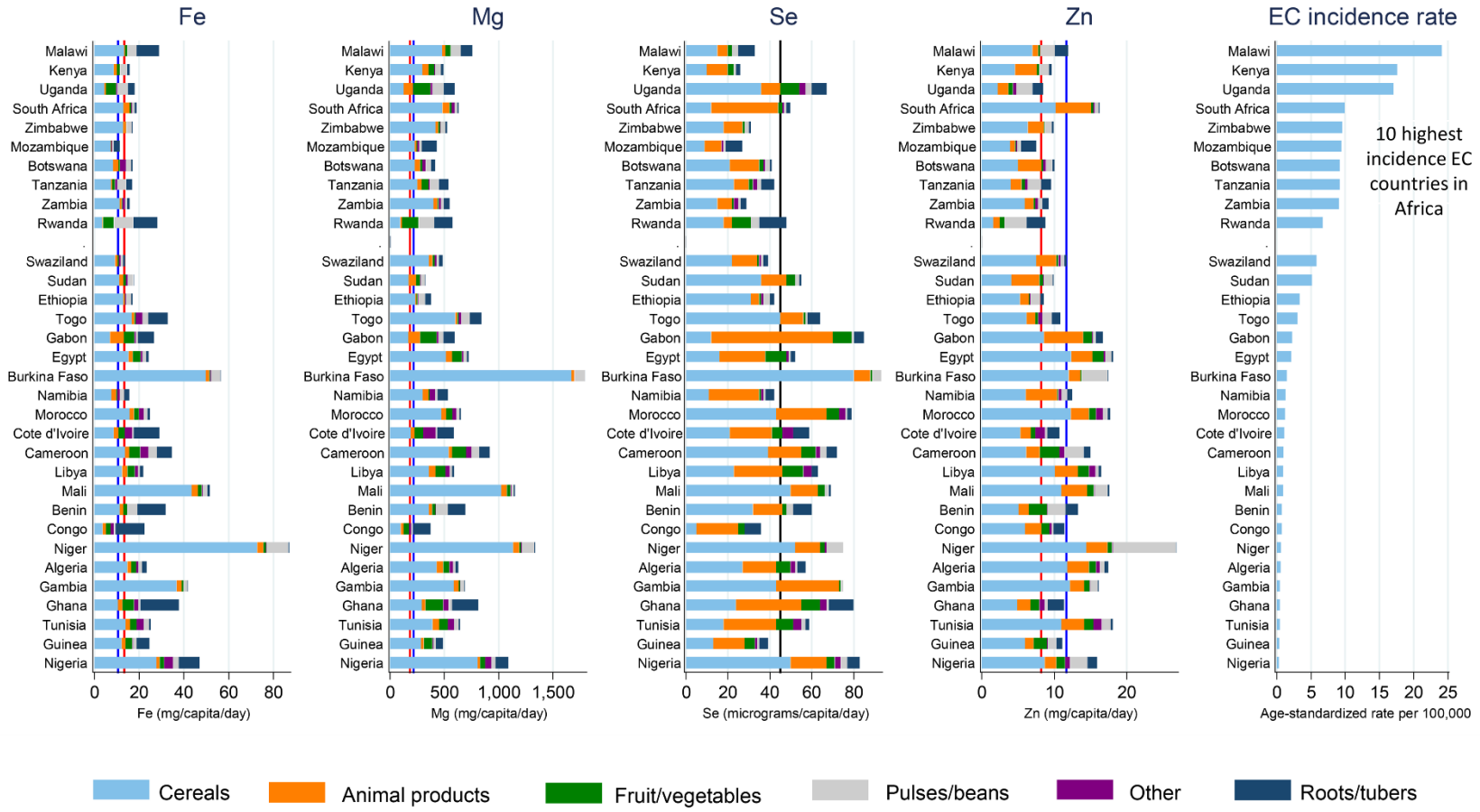


Suggestions of Micronutrient deficiencies



Hurst R. Scientific Reports 2013

National nutrient supplies per capita across Africa, separating 10 highest EC incidence countries



International Agency for Research on Cancer

World Health Organization

Joy et al. Dietary mineral supplies in Africa. Physiol Plant 2014;151:208-29; Schaafsma et al. Plos One 2015

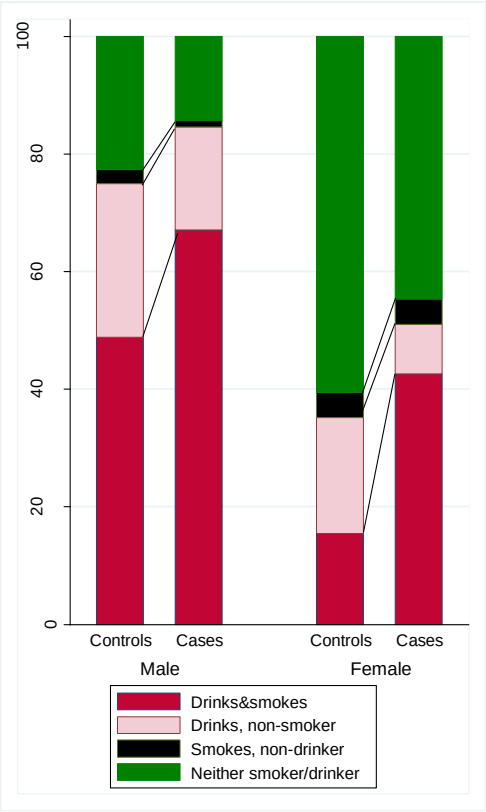
ESCCAPE

Eldoret – Pilot study

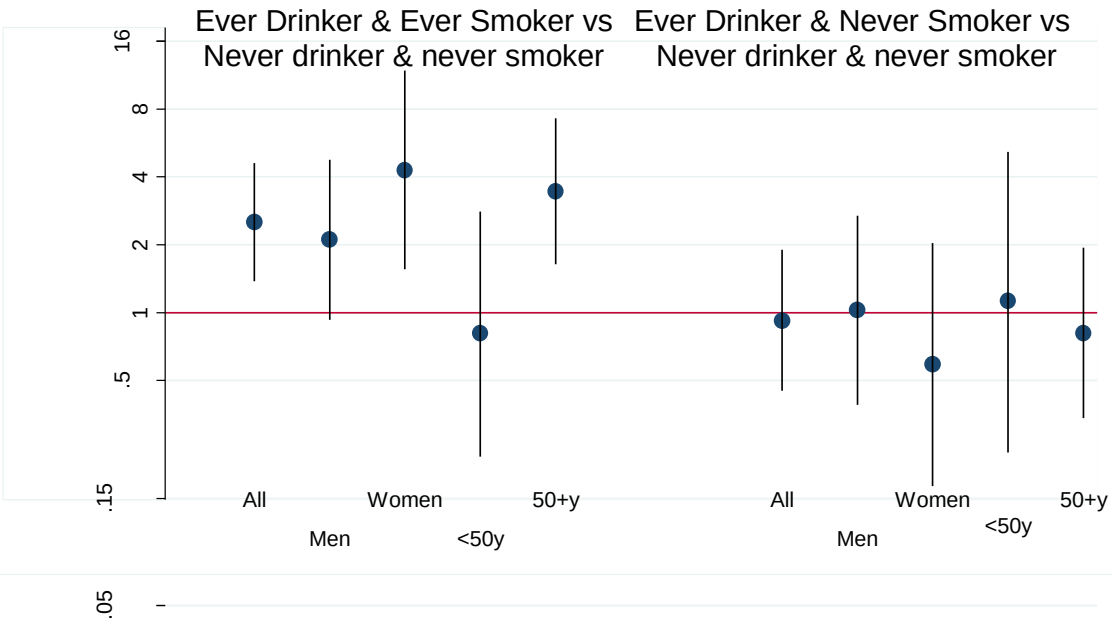
- 164 case-control pairs (84% ESCC). Non-ESCC excluded

	Cases N=138	Controls N=155
Male (col %)	66 %	54 %
Age: mean, range	58 (28-89)	56 (21-91)
No. children (median)	6	6
Family history EC	2.2 %	3.9 %
Farmer Office/business Other	62 % 30 % 8 %	50 % 42 % 8 %
Kelenjin Luhya Luo Other	59 % 25 % 8 % 8 %	53 % 21 % 10 % 16 %

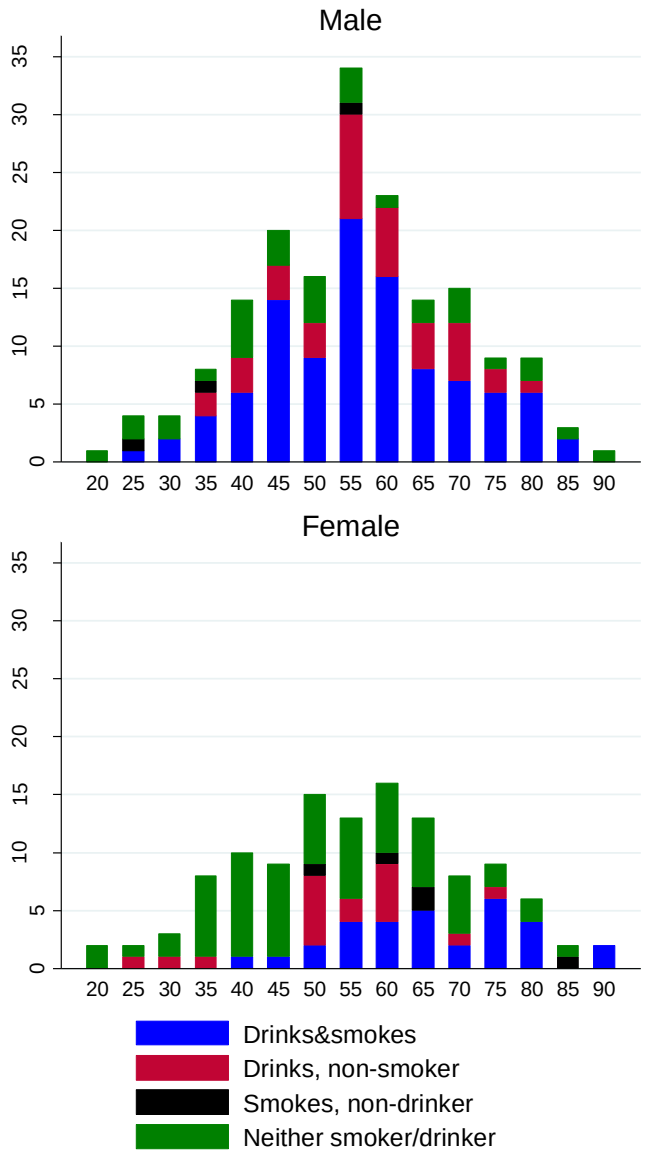
Combined alcohol and smoking



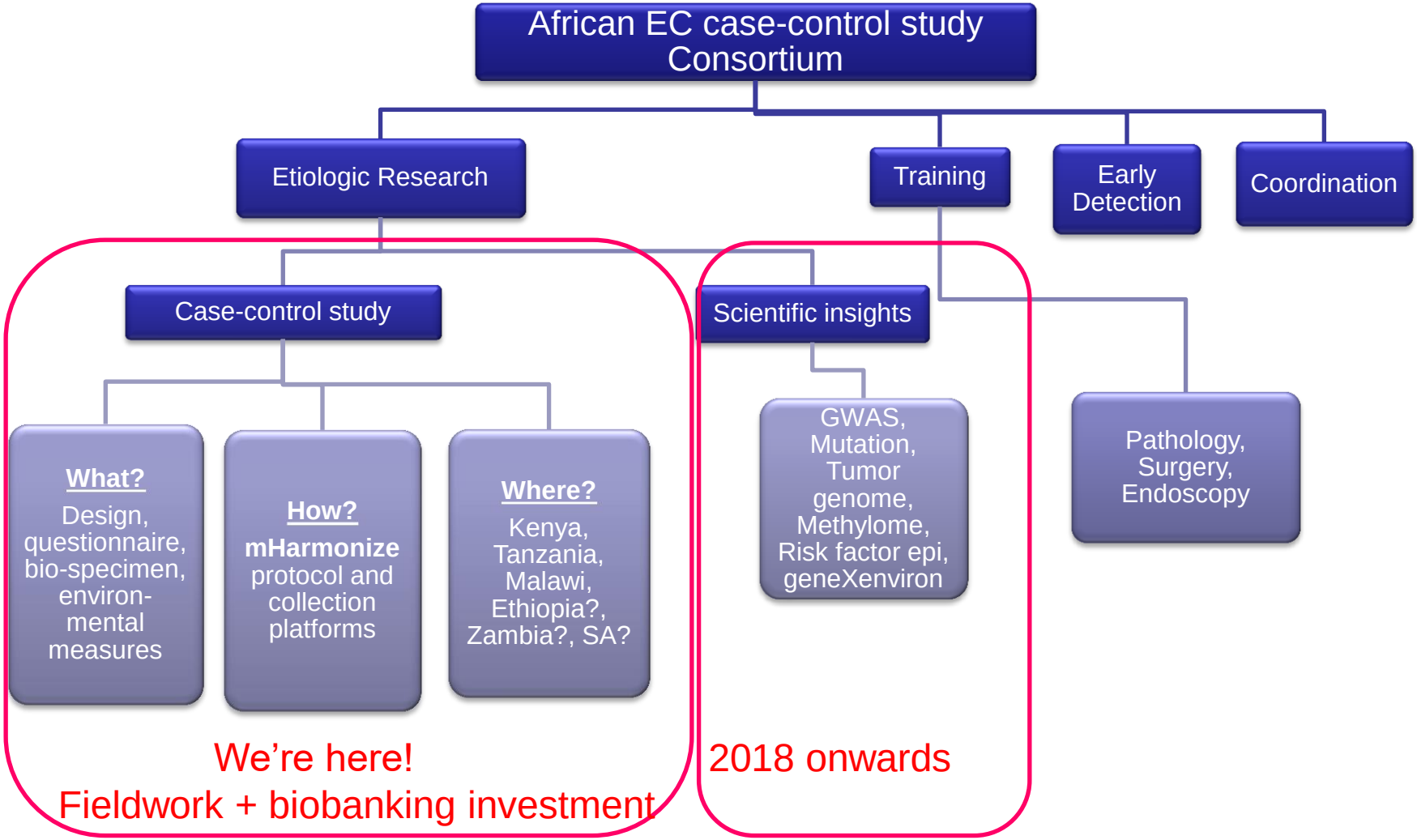
Cases



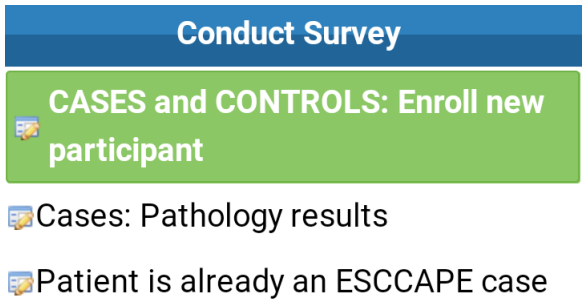
ORs adjusted for age, gender; P-interaction with age for drink+smoke significant

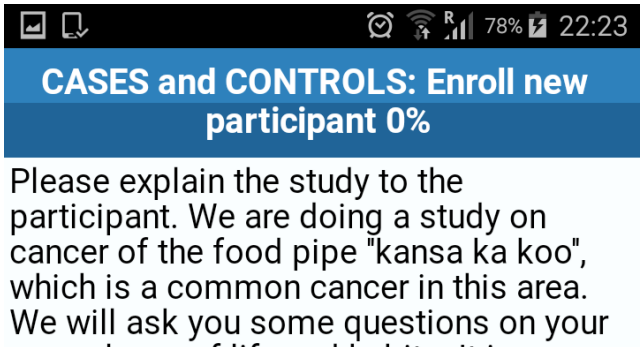


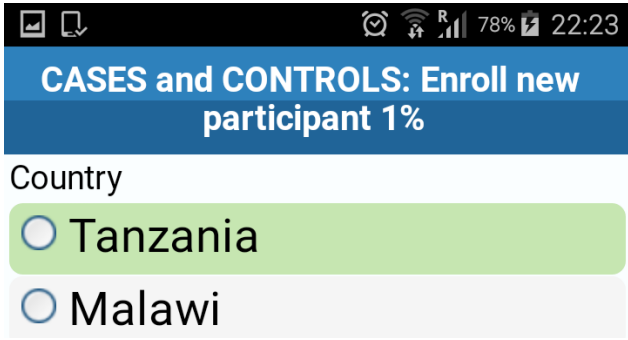
Graphs by survey-gender

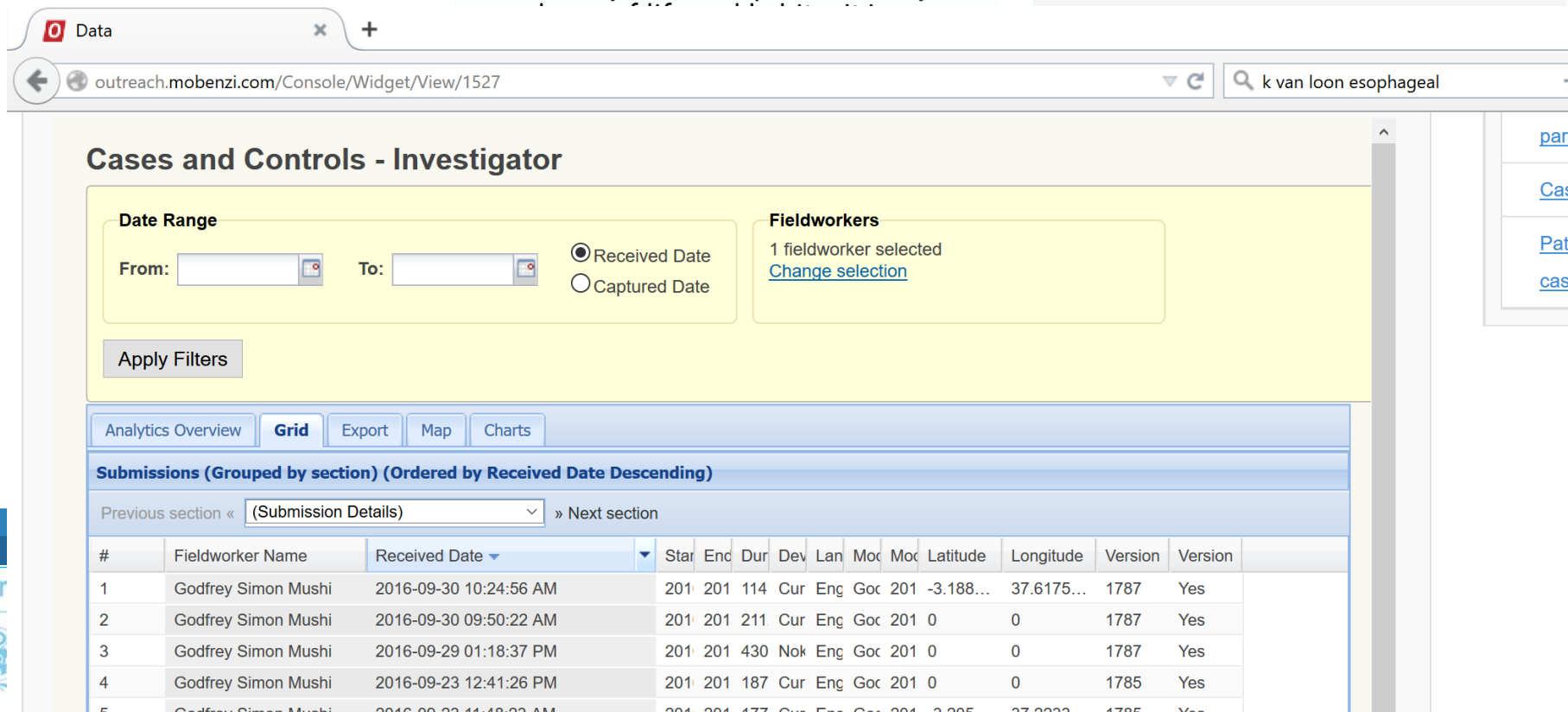

African EC case-control study Consortium
Etiologic Research
Training
Early Detection
Coordination
Case-control study
Scientific insights
What?
Design, questionnaire, bio-specimen, environ-mental measures
How?
mHarmonize protocol and collection platforms
Where?
Kenya, Tanzania, Malawi, Ethiopia?, Zambia?, SA?
GWAS, Mutation, Tumor genome, Methylome, Risk factor epi, geneXenviron
Pathology, Surgery, Endoscopy
We're here!
Fieldwork + biobanking investment
2018 onwards

mHealth Harmonized data collection from the outset









No. case-control sets – full detailed questionnaire + tumor + DNA

	KE Eldoret	KE Tenwek	TZ Moshi	TZ Dar	ML Lilongwe	All
To end 2016	300	70	100	400	-	870
2017	150	200	100	-	100	550
2018	?	200	100	-	100	400
To end 2018	450	470	300	400	200	1820

No. case-control sets – short questionnaire + tumor + DNA

	KE Eldoret	KE Tenwek	TZ Moshi	TZ Dar	ML Lilongwe	All
To end 2016	300	70	100	400	-	870
2017	150	400	100	400	100	1050
2018	?	400	100		100	500
To end 2018	450	870	300	800	200	2620

Team Effort

Eldoret
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M. Oduor

Moshi
B. Mmbaga
A. Mwasamwaja
G. Mushi
M. Oresto Munishi

Malawi
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Consortium
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C. Carreira, IARC
M. Watts, BGS C. Abnet, NCI
S. Dawsey,NCI
G. Murphy, NCI
N. Pritchett, NCI
B. Kaimila, UNC Lilongwe
S. Gopal, UNC Lilongwe
M. Mwachiro
K. Van Loon, UCSF

Questions

- How to attract funding?
- How to investigate nutritional deficiencies in case-control design?
- What is the appropriate control group?
- Where to locate studies? Incidence gradient undefined.
- Is South Africa part of the ESCC corridor?
- Drivers in women, non-drinkers/non-smokers, young cases
  - Continue recruitment < 40 cases?