

## Esophageal Squamous Cell Carcinoma African PrEvention research (ESCAPE)



- East African 3-country case-control studies: 1300 cases, 1300 controls, with: Moi University, **Kenya**; Kilimanjaro Clinical Research Institute **Tanzania**; College of Medicine **Malawi**; US NCI; Universities of Liverpool and Cambridge
- Putative setting-relevant risk factors
 

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|--------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>• Geophagia</li> <li>• Mswaki stick</li> <li>• Khat</li> <li>• Hot tea</li> </ul> | <ul style="list-style-type: none"> <li>Mursik (milk)</li> <li>Household air pollution</li> <li>Micronutrient deficiencies</li> <li>Early-life exposures</li> </ul> | <p style="color: green; margin: 0;"><u>Subsets of interest</u></p> <ul style="list-style-type: none"> <li>Women</li> <li>&lt; 40 year patients</li> <li>Never alcohol+tobacco users</li> </ul> |
|--------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
- 2019 fieldwork:
  - **HAP-ESCAPE**: 24-hour **H**ousehold **A**ir **P**ollution monitoring in case-control study
  - **HOT-ESCAPE**: **H**ot beverage/porridge temperature measurements
  - **CytoSCCAPE**: First pilot study of the Cytosponge™ pill-on-a string device in Africa. Acceptable non-endoscopy esophageal cell collection method.

<http://esccape.iarc.fr/>

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East Africa has extremely high incidence and mortality rates from oesophageal cancer, similar to the Asian oesophageal cancer belt. IARC is leading aetiological studies across East Africa, aimed to comprehensively study a variety of potential setting-specific contributors. We are studying lifestyle factors, living conditions, environmental factors and susceptibility and tumour genetics. At present, 1300 cases and 1300 controls across Kenya, Tanzania and Malawi have been recruited (approximately 90% before completion), representing the largest effort of this kind to date.

A strong focus on exposures local to these settings and cultures is being emphasized e.g. traditional brews and distillations, geophagia, cleaning teeth with charcoal and a chewed stick, thermal injury (with the consumption of hot tea at high altitudes), household air pollution commencing early in the life-course, contaminated foods and smokeless tobacco.

The study represents a strong collaboration with 3 African universities. The study personnel in East Africa have benefitted from IARC summer schools (7 attendees), 2 very productive UICC-IARC development fellows and postdoctoral fellows. Findings from Kenya up to today confirm the contribution of alcohol consumption to the oesophageal cancer burden, as well as suggest local habits of drinking hot beverages and different indicators of poor oral health; all are modifiable risk factors.

In 2019, IARC, in collaboration with the University of Cambridge, also initiated Africa's first study of the acceptability of using the cytosponge pill-on-a-string device for oesophageal cell collection. The study demonstrated high acceptability and feasibility in Tanzania, which now opens a new avenue for aetiological and early detection research using this cheap appropriate-health technology (AHT) for the collection of oesophageal cells and thus investigation of drivers of potential early mutations.



- **AGRICOH**: international consortium of **30 agricultural cohorts** from **13 countries**
- Aims: investigate the associations between agricultural exposures and health outcomes, including cancer, through international collaboration
- Findings to date: Most pesticides not associated with an increased risk of Non-Hodgkin lymphoma (NHL), but suggestions of an association with terbufos and deltamethrin, and – lesser so – with glyphosate; based on large cohorts from the USA, France and Norway (totalling 316,000 farmers)
- Ongoing projects: Cancer incidence among farmers, pesticide use in association with myeloid malignancies, with breast cancer, and with prostate cancer

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<http://agricoh.iarc.fr/>

Because of their chemical properties, several pesticides are suspected to increase the risk of cancer, which – because of their widespread use – is important for cancer prevention. Worldwide, an estimated 866 million people are officially employed in the agricultural sector. While agricultural work contributes to a large part of employment and economic resources in many countries, the nature of work can pose some occupational hazards due to intense physical labour and exposures to potentially hazardous substances including pesticides, fertilizers, solvents, solar ultraviolet radiations, diesel exhaust fumes. To ensure the safety of the workers, it is important to understand health risks associated with these hazards.

AGRICOH, an international consortium of agricultural cohort studies, was established in 2010. The consortium currently consists of 30 agricultural cohorts from 13 countries. AGRICOH aims to promote and sustain collaboration and pooling of data to study a wide range of agricultural exposures and health outcomes including cancer.

Findings to date showed that most pesticides investigated were not associated with an increased risk of Non-Hodgkin lymphoma (NHL), a cancer previously reported to be more common among farmers. The exception was the use of terbufos showing a modestly increased NHL risk, and deltamethrin and – to lesser extent – glyphosate were modestly associated with NHL subtypes.

Within the working group of cancer outcome, there are currently four further projects underway, namely an ecological study of cancer incidence rates and studies of pesticides in relation to myeloid malignancies, breast cancer, and prostate cancer.

## Asbest Chrysotile Cohort Study

- Cohort of study of workers exposed to chrysotile asbestos in mines and enrichment factories in Asbest, Russian Federation, the world's largest active asbestos mine
- Cohort includes 35,837 workers (37% women) with dust measurements; of those 12,729 have died (2,373 of cancer)
- ✓ Largest cohort of asbestos miners and millers in the world
- ✓ First miners and millers cohort with female workers exposed to chrysotile
- ✓ Risk analysis carried out 2020-21

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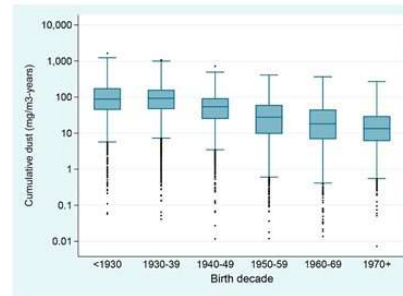


Figure. Cumulative dust exposure by birth cohort

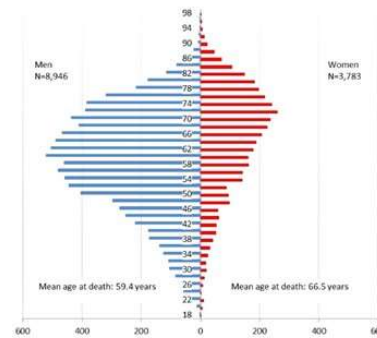


Figure. Age pyramid of deaths among cohort members

<http://asbest-study.iarc.fr/>

The Asbest Chrysotile Cohort Study was started in 2012 to investigate cancer mortality in workers exposed to chrysotile asbestos in the world's largest active asbestos mine in Asbest, Sverdlovsk region, the Russian Federation. The cohort includes 35,837 workers in the mines or enrichment factories, active between 1975 and 2015, followed up for vital status until 2015. Notably, 37% of workers were women, showing comparable levels of exposures to men.

The cohort is now the worldwide largest cohort study of miners and millers, and the first that allows investigating cancer mortality in women. The latter is of high interest for lung cancer as smoking rates are lower in women and for all gynaecological cancers. Exposure is estimated from regular dust measurements at the work places that were carried out for the last approximately 80 years.

Graphs show that while dust exposures decline over time with the highest exposures among those born before 1940, there is also exposure variability among those born later. Among the 12,729 deaths observed in the cohort, the average age at death among men was relatively young.

Risk analysis will be carried out in 2020 to 2021.



## Research related to the Chernobyl nuclear accident

- Providing understanding of cancer risk after protracted low-dose exposure to ionizing radiation for radiation protection
- Studying the role of host and environmental factors, including determinants of individual susceptibility to radiation-induced cancers
- Recent findings confirmed that the radiation-related thyroid cancer risk in subjects who did not receive stable iodine supplementation in the years after the accident was higher than in those receiving supplementation
- **Aiming at**
  - Overcoming the standstill of the **Chernobyl research agenda**
  - Tailoring **early detection/ prevention** efforts to higher risk populations after the accident
  - Further **improvement** of international **radiological protection**
  - Improving **risk communication** in populations affected by nuclear accidents

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<http://co-cher.iarc.fr/>

Even 34 years later, the Chernobyl nuclear accident continues to cause fears and myths about its health consequences. While many open questions remain, declines in funding caused an unfortunate decline in research. IARC researchers recently published an appeal in *The Lancet* (“Future of Chernobyl research: the urgency for consolidated action”) to overcome the standstill of the Chernobyl research agenda, urgently needed due to the aging of affected populations.

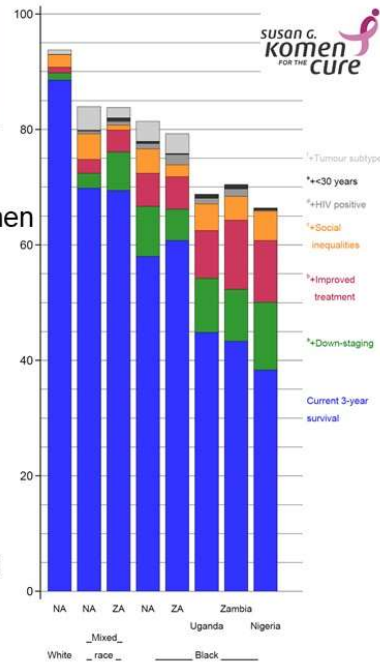
At the same time, IARC continues some studies on cancer risks in Chernobyl populations, those exposed in childhood and adolescence in the Russian Federation and Belarus, and in female residents of the most radioactively contaminated territories in Ukraine and Belarus. The special attention is given to host and environmental factors that could determine individual susceptibility to radiation-induced cancers. Recent findings confirmed that the radiation-related thyroid cancer risk among people exposed to radioiodine as children and adolescents who did not receive stable iodine supplementation in the following years was higher compared to the people who received stable iodine.

Evidence on cancer risks from exposure to ionizing radiation (IR) at low levels after Chernobyl are of international significance because of increasing numbers of exposed to low dose IR from medical sources, and in case of potential future nuclear accidents. They contribute to the evidence base used by international and national health and radiation protection authorities adjusting health surveillance of the affected populations, improving radiological protection and strengthening risk communication.

## African Breast Cancer – Disparities in Outcomes (ABC-DO) Study Survival Gap Apportionment in Africa



- 5-country hospital-based cohort of 2200 women
- 3 year survival ranges from **<40% to >90%**
- Low survival is **largely modifiable**, through near equal contributions of **down-staging and quality treatment access**
- Lower survival is associated with HIV+ women, non hormone-receptor positive tumours and young patients, but have limited contribution to low survival



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NA = Namibia ZA = South Africa

<http://abc-do.iarc.fr/>

Premature cancer deaths in sub-Saharan Africa disproportionately affect women, e.g. there are 180 deaths in women for every 100 deaths in men at ages 40-54 years. This excess is largely due to breast and cervical cancer. Whilst cervical cancer is being tackled through prevention, the strongest risk factors for breast cancer (late and low parity) are rare. Instead the major avenue for the reduction in breast cancer deaths in this region will be through improving survival rates.

In 2014, supported by Susan G Komen, IARC undertook the first multi-centre prospective study of breast cancer survival (ABC-DO) to robustly study survival rates and conduct survival gap apportionment analyses. In the graph provided, in blue, we see that 3-year survival rates vary greatly and are as low as about 40% in the Nigerian settings, and at most 60% in black women in Southern Africa. These compare to 90% at 5 years in Europe, i.e. representing a large burden of avoidable deaths. Analyses of the contributors to low survival unsurprisingly revealed the impact of late stage at diagnosis (green), reflecting inadequacies in the referral system to a cancer diagnostic and treatment centre. Treatment gaps equally contributed to the survival gap, highlighting that access to high quality and complete treatment access needs to be improved, representing a cost effective approach to reducing breast cancer deaths in this setting.

ABC-DO has also provided valuable insights into weak nodes in the pre-diagnostic journey, information on quality of life, treatment side-effects, the impact of HIV on a common non-HIV-associated malignancy, and on maternal orphans of cancer.

# World Code against Cancer



✓ Set of cancer prevention recommendations  
 ✓ Suited to the regional epidemiological, economic, social, and cultural conditions  
 ✓ Adapted to different audiences and dissemination channels

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 World Health Organization  
<http://cancer-code-europe.iarc.fr/>



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- 1) Effective **communication** of latest evidence
- 2) Empowering communities while offering good **framework** for prevention program
- 3) Strong **evidence** base and regional data
- 4) **Ownership** and political impact
- 5) **United** voice to call for cancer prevention

The features of the World Code against Cancer are:

- Authoritative, clear and evidence-based recommendations to promote cancer prevention
- Regional Codes against Cancer under the umbrella of a World Code against Cancer
- Equally valuable for health professionals, policy-makers and the general public worldwide

It is estimated that 40% of cancer cases can be prevented and further mortality could be reduced. The European Code against Cancer stood out as an integrated instrument for cancer prevention that informs how to avoid or reduce exposures to known causes of cancers, to adopt behaviours to reduce cancer risk, and to participate in vaccination and screening programmes under the appropriate national guidelines.

The development of a set of cancer prevention recommendations suited to the different regional epidemiological, socio-economic and cultural conditions offers an exceptional public health tool to guide and support governments in the implementation of their cancer control strategies, as well as to educate the population on healthy behaviours and encourage participation in prevention programmes. Regional Codes would focus on areas sufficiently large but also distinct enough to merit the development of individual versions.

The World Cancer Code will improve cancer prevention (1) by promoting effective communication of scientifically up-to-date and validated evidence; (2) by stimulating the empowerment of communities while offering a good framework for prevention education programs; (3) by offering a strong evidence base and regional data; (4) by facilitating ownership and political impact through the endorsement of the countries of a region; and (5) by providing a united voice to call for cancer prevention. In addition, it contributes to Sustainable Development Goals (SDG) by reducing the total premature mortality (SDG 3), by promoting safe working environment (SDG 7), by minimizing the adverse health effects of chemicals (SDG 12.4), and by enhancing international collaboration (SDG 17.6).