

WHO perspective on the contribution of academic clinical laboratories in cancer research

International Agency for Research on Cancer Lyon, France

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Role of laboratory medicine in the fight against cancer 15th October 2022

The IARC at the WHO

IARC was created in 1965 by the World Health Organization (WHO)

It is the executive research Agency of WHO with a focus on cancer

IARC performs cancer research for cancer prevention with an international perspective

- 1. Interdisciplinary (e.g. epidemiological and laboratory-based)
- 2. Inclusive of LMICs
- 3. Intended to inform public health decisions and policies
- 4. Intended to inform guidelines and standards



Classification of tumors

WHO Classification of Skin Tumours

Edited by David E. Elder, Daniela Massi, Richard A. Scolyer, Rein Willemze



WHO Classification of Tumours • 5th Edition

Digestive System Tumours

Edited by the WHO Classification of Tumours Editorial Board





Classification of substances

WORLD HEALTH ORGANIZATION INTERNATIONAL AGENCY FOR RESEARCH ON CANCER IARC Monographs on the Evaluation of **Carcinogenic Risks to Humans VOLUME 94 Ingested Nitrate and Nitrite and Cyanobacterial Peptide Toxins** LYON, FRANCE 2010

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There is sufficient evidence the agent causes cancer in humans.

IARC Classifications

evidence the agent causes

WHAT IT MEANS

There is sufficient

cancer in humans.

Anabolic steroids, high temperature frying, HPV, red meat, Roundup (glyphosate), Actos (pioglitazone), N-nitrosodiethylamine (NDMA)

Solar radiation, processed

asbestos, talc-based baby

powder contaminated with

EXAMPLES

asbestos

meats, alcoholic

beverages, smoking,

Probably Carcinogenic to Humans

Group

 $2\mathbf{R}$

Possibly Carcinogenic

Group

to Humans

Group

GROUP

Group

Carcinogenic to

Humans

Limited evidence in humans and less than sufficient evidence in animals. Aloe vera leaf extract, marine diesel fuel, gasoline, engine exhaust, Asian pickled vegetables, progestin, perineal use of talc-based body powder

Evidence is inadequate in humans and inadequate or limited in animals. Coffee, low-frequency electric fields, dental materials, ceramic implants, chlorinated drinking water, tea, printing inks

Not Classifiable as to its Carcinogenicity in Humans

Evaluation of less than 3 doses of HPV vaccination in India

Mean MFI values for HPV 16 antibodies at different time points and under different vaccine schedules



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World Health Organization among girls who completed vaccination per protocol vaccination at day 1, 60 and 180 (3-dose group) vaccination at day 1 and 180 (2-dose group) among girls who did not have their complete vaccine schedules vaccination at day 1 and 60 vaccination with a single dose

Seropositivity cutoff

Sankaranarayanan R et al. Lancet Oncol. 2016;17(1):67-77

Frequency of persistent HPV 16 and HPV18 infection in vaccinated and unvaccinated women

Vaccination schedule	Nº of subjects	Nº of HPV 16/18 infections
	241	0
	224	0
	365	0
1-Dose	405	0
All vaccinated girls	1235	0
Unvaccinated women	738	6 (0.8%)

Supported by the Bill & Melinda Gates Foundation Vaccines provided by Merck

Supporting the Precision Medicine vision

New Paradigm Shift in Treatment

Transitioning From the 'one-size-fits-all' to 'precision medicine' model with multi-level patient stratification.



Reference: Precision Medicine Alliance 2017



WHO report on cancer (2020)



WHO report on cancer (2020)

All cancer treatment plans and the vast majority of medical decisions for cancer patients rely on quality pathology and laboratory medicine



Fig. 4.2. Steps in cancer early diagnosis.



The laboratory 'user demands' have expanded

The development of Biomedical laboratories over the last 20 years summarised as follows:

- Laboratory 1.0
 Focus on the expertise, supply lines, protocols
- Laboratory 2.0 Focus on quality of processes, rising costs and reproducibility of results
- Laboratory 3.0 Introduce computers, mechanical processes and automation, increase scale and turnaround times
- Laboratory 4.0 (now) Digital infrastructure, increased efficiency, intelligent decision support systems



Data underpins personalised medicine

- Healthcare is seeing the largest increase in data use y-o-y



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<u>Reference</u>: Coughlin S, et al. Looking to tomorrow's healthcare today: a participatory health perspective. Internal medicine journal. 2018; 48(1):92-6.

Data underpins personalised medicine - The COVID-19 impact



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<u>Reference</u>: Coughlin S, et al. Looking to tomorrow's healthcare today: a participatory health perspective. Internal medicine journal. 2018; 48(1):92-6.

Specific examples



Focus on quality data for stratification

Detailed stratification is key to developing diagnostics, e.g. the European Prospective Investigation into Cancer and Nutrition study (EPIC; <u>https://epic.iarc.fr/</u>)





Detailed stratification



Figure 3 Recalibration plots of colorectal cancer risk models within the European Prospective Investigation into Cancer and Nutrition. Time horizon was 10 years for all models except Steffen *et al* which was 5 years.¹⁰

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<u>Reference</u>: Smith, Todd, et al. "Comparison of prognostic models to predict the occurrence of colorectal cancer in asymptomatic individuals: a systematic literature review and external validation in the EPIC and UK Biobank prospective cohort studies." Gut 68.4 (2019): 672-683.

Detailed genomic data for Mutographs of cancer

Genomes of 5,000 pancreatic, kidney, oesophageal and bowel cancer patients from five continents will be studied and their mutational signatures compared

https://www.sanger.ac.uk/colla boration/mutographs-cancercruk-grand-challenge-project/

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World Healt

Organization



30 cancer mutational signatures

Genomic signature of renal carcinomas



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<u>Reference</u>: Jelaković, Bojan, et al. "Renal cell carcinomas of chronic kidney disease patients harbor the mutational signature of carcinogenic aristolochic acid." International journal of cancer 136.12 (2015): 2967-2972.

Genomic signature of renal carcinomas



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World Health Organization <u>Reference</u>: Ng, Alvin WT, et al. "Aristolochic acids and their derivatives are widely implicated in liver cancers in Taiwan and throughout Asia." Science translational medicine 9.412 (2017).

Leverage existing cohorts for large-scale research

Fig. 1: Overview of the patient populations with CRC included in this study and their associated gut microbiome compositions.



Multi-kingdom microbiota analyses identify bacterial–fungal interactions and biomarkers of colorectal cancer across cohorts

Liu, Ning-Ning, et al. Nature microbiology 7.2 (2022): 238-250 Agency for Research on Cancer





A polygenic risk score for nasopharyngeal carcinoma shows potential for risk stratification and personalized screening

He, YQ, et al. Nature communications 13.1 (2022): 1-10.

How do we engage academic clinical laboratories in LMIC?



Inclusiveness of LMICs: BCNet

Biobank and Cohort Building network:

- A research-ready infrastructure network within LMICs
- Harmonisation of processes and training on Biobanking standards and SOPs
- Ongoing support through online educational portal (biobanklearning.iarc.fr)



Developing Standards and Best Practices

A significant, co-ordinated effort over the last years



2017

2018

2019







Identifying knowledge gaps and priorities

Mini Review





A million Africans a year dying from cancer by 2030: what can cancer research and control offer to the continent?

Bakary S. Sylla and Christopher P. Wild

International Agency for Research on Cancer, 69372 Lyon, CEDEX 08, France

In Africa, there were an estimated 681,000 new cancer cases and 512,000 deaths in 2008. Projections to 2030 show a startling rise, with corresponding figures of 1.27 million cases and 0.97 million deaths resulting from population growth and aging alone. The figures make no assumptions about incidence rates which may increase due to the further introduction of tobacco and a more westernized lifestyle. The current situation in many parts of Africa with respect to health care systems suggests that improved cancer treatment would be an insufficient response to this increasing burden. Much could be achieved through cancer prevention by applying current knowledge about major risk factors and the natural history of the disease. For example, vaccination against hepatitis B virus and human papilloma viruses would prevent the occurrence of two of the most common cancers in Africa, liver and cervix, respectively, in the long-term. Strong measures to prevent the widespread introduction of tobacco must be a priority. Early detection and treatment of cervical and breast cancers using

- □ Awareness
- □ Funding
- Description
- □ Training
- International collaboration
- Establish ethics committees

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Table 2. Ten priorities and actions for cancer research and control in Africa

- 1. Increased cancer awareness by governments, planners, leaders and their people
- 2. Adequate funding, with defined budget line, for national cancer control programmes
- 3. More extensive and accurate description of the cancer burden
- 4. Prioritised research into the causes and prevention of cancer

5. Promotion of primary prevention (tobacco control; HBV and HPV vaccination; prevention of blood-borne virus transmission; control of sexually transmitted disease)

- 6. Introduction of screening and early detection (cervix, breast)
- 7. Access to basic diagnostic and treatment services including affordable radiotherapy, anti-cancer drugs as well as palliative care

8. Planned training and retention of health care professionals and researchers

9. Promotion of international collaborations in partnerships of equals

10. Establishment of national and regional ethics committees to ensure respect for patients and participants

Post-pandemic, somewhat improved granularity

Panel 1: Summary of identified registry and infrastructure challenges in sub-Saharan Africa, and potential recommendations to address them

Leadership and coordination systems⁹

- Strengthen dedicated leadership training
- · Align registries coordination with national health systems
- Enhance stakeholder input, recognition, and feedback mechanisms

Absence of harmonised standards⁴⁵

- Install harmonised documentation forms for uniform data collection across data sources
- Use large cancer treatment centres in capital cities as exemplars, setting the standards

Insufficient funding^{40,42,44,45}

- Introduce clear and transparent lines of budgetary support
- Advocate governmental and stakeholder long-term support and commitment

Research ethics and confidentiality⁴²

- Set a transparent data governance policy
- Support legal permission to register all cancer cases over time
- Increase data safety and security

Absence of diagnostics facilities⁴⁰

- Strategic prioritisation of achievable goals
- Leverage eHealth solutions for remote diagnostic capabilities

Ngwa, Wilfred, et al. "Cancer in sub-Saharan Africa: a Lancet Oncology Commission." *The Lancet Oncology* (2022).



Post-pandemic, LMIC cohorts and biobank specifics

Table 1

The five priority aspects identified for infectious diseases biobanks in LMICs, with the related challenges and enablers.

Priority	Challenges	Enablers
Equipment	 Legacy equipment Interoperability Equipment maintenance 	 Synergies with existing initiatives/infrastruc- tures 'Tropicalized' equipment
Laboratory	- Legacy systems	- Open access software
Management	 Consistent data 	- Staff training
Information	input	- Data quality indicators
Systems (LIMS/ BIMS)	- Data quality	
Customised training	- Lack of core mate-	- Dedicated LIMC courses
materials	- Cost of training	- Utilizing existing resources
Skilled laboratory staff	 Low staff numbers High staff turnover Competing priorities 	 Synergies with existing initiatives/infrastruc- tures Staff incentives
Regulatory frameworks for samples and data collection/sharing	 Different frame works for samples and data collection/ sharing Lack of appropriate legal/ethical 	 Introduction of expert consensus where frame- work is absent Highlighting gaps in legal/ethical frameworks

Ezzat S, Biga R, Kozlakidis Z. Biobanking in LMIC settings for infectious diseases: Challenges and enablers. Biosaf Health. 2022 Jul 25. doi: 10.1016/j.bsheal.2022.07.002.



What type of samples?

	Stored samples by type	Stored samples in participating centres by storage condition					
		room temp.	refrigerated	d −20°C	-80°C	cryofreeze	temp. not listed
Blood	63% (12/22)	2/22 (9%)	2/22 (9%)	0%	8/22 (36%)	0	2/22 (9%)
Blood-derived products	78% (17/22)	0	3/22 (14%)	3/22 (14%)	9/22 (41%)		2/22 (9%)
Bone marrow	10% (2/21)	0	0	0	0	0	2/21 (10%)
Frozen tissue	38% (8/21	0	0	0	4/21 (19%)	1/21 (5%)	3/21 (14%)
Tissue slides	59% (13/22)	8/22 (36%)	0	0	1/22 (5%)	0	4/22 (18%)
Paraffin-embedded tissue blocks	68% (17/25)	13/25 (52%)	ø	0	0	0	4/25 (16%)
Formalin-fixed tissue	50% (12/24)	8/24 (33%)	0	0	0	0	4/24 (17%)
Cell lines	10% (2/21)	0	0	0	1/21 (5%)	0	1/21 (5%)
Cord blood	15% (3/20)	1/20 (5%)	0	1/20 (5%)	1/20 (5%)	0	0
DNA samples	68% (15/22)	0	0	5/22 (23%)	8/22 (36%)	0	2/22 (9%)
RNA samples	50% (11/22)	0	0	4/22 (18%)	6/22 (27%)	0	1/22 (5%)
Sperm	10% (2/20)	0	0	1/20 (5%)	0	1/20 (5%)	0
Others (urine, buffy coat, body fluids)	77% (16/21)	0	0	2/21 (10%)	9/21 (43%)	3/21 (14%)	2/21 (10%)

Mendy, M, et al. "Infrastructure and facilities for human biobanking in low-and middle-income countries: a situation analysis." *Pathobiology* 81.5-6 (2014): 252-260.



What type of data?

Of what quality?



A data-driven future for clinical laboratories





• The future is:

Data-based, data-driven and to some extent be vendor-agnostic

• Families of standards around laboratory data are likely to emerge, complementing existing ones





- The regulatory development in LMICs has been rapid, but problematic in terms of trans-regional/trans-national compatibility

Country	Title	Year	Refs.
Ethiopia	National Research Ethics Review Guidelines	2014	51
Ghana	Public Health Act	2012	45
	Data Protection Act	2012	79
Kenya	Guidelines for Ethical Conduct of Biomedical Research Involving Human Subjects	2004	46
	The Health Laws (Amendment) Act	2019	47
Nigeria	Policy Statement on Storage of Human Samples in Biobanks and Biorepositories	2013	53
0	National Health Act	2014	49
Sudan	National Guidelines for Ethical Conduct of Research Involving Human Subjects	2008	50
South Africa	The National Health Act	2003	55
	Regulations Relating to the Use of Human Biological Material	2012	56
	Protection of Personal Information Act	2013	78
	Ethics in Health Research: Principles, Processes, and Structures	2015	57
Tanzania	The Human DNA Regulation Act	2009	43
	Guidelines of Ethics for Health Research in Tanzania.	2009	44
Thailand	Ethical Guidelines for Research on Human Subjects	2007	52
The Gambia	Guidelines of the National DNA Bank	2001	63
Uganda	National Guidelines Involving Humans as Research Participants	2014	61
	Data Protection and Privacy Act	2019	80
Zambia	National Health Research Act	2013	41
Zimbabwe	Medical Research Council of Zimbabwe. Adult Consent Form.	2013	65

TABLE 2. LIST OF THE DOCUMENTS USED IN THIS NARRATIVE REVIEW, ARRANGED BY COUNTRY

Reference: Vodosin P, et al. on behalf of the BCNet members. Biopreservation and Biobanking. ahead of print http://doi.org/10.1089/bio.2020.0101





GENERAL ORGANISATION IN AFRICA	ETHICAL AND REGULATORY EDAMEWODY
	LANGUAGE CONSTRAINTS
	ASSOCIATED DATA COLLECTION SYSTEM
	MANAGEMENT OF THE ASSOCIATED DATA FLOW
	CONCLUSION AND PERSPECTIVES
	BIBLIOGRAPHY
	WEBOGRAPHY

COMESA	
CENIAC	
53400	
CIENN-SSAAD	
Saharan Africa	
Saharan Africa	

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Nissa FOUNAS

Albion KOLGECI

ECI

Vincent SEMERARO

Elsa ZULIANI



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Nissa FOUNAS

Albion KOLGECI

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Languages	
French	
English	
Portuguese	
Other	
Outside Sub-Saharan Africa	

Map illustrating the various languages spoken in sub-Saharan Africa.

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Nissa FOUNAS

Albion KOLGECI

GECI

Vincent SEMERARO

ETHICAL AND REGULATORY FRAMEWORK

LANGUAGE CONSTRAINTS ASSOCIATED DATA COLLECTION SYSTEM

MANAGEMENT OF THE

ASSOCIATED DATA FLOW CONCLUSION AND

> PERSPECTIVES BIBLIOGRAPHY

WEBOGRAPHY

Setting a strong foundation in ASEAN

- A glossary of terms has been constructed in ASEAN member states paving the way for a common understanding, before further translations take place

ISBER BP/ISO20387/Both	Hindi	Indonesian	Vietnamese	Japanese
accessioning	परिग्रहण करना	menerima, mendapatkan	quyền truy cập	アクセスする
acquisition	अभिग्रहण,अर्जन,प्रप्ति		mua lại, thâu tóm	取得
ALIQUOT (ALIQUOTED, ALIQUOTING)	विभाज्य	aliquot, cuplikan		アリコート
Aliquoted	बनाया गया विभाज्य	dialiquot, dicuplik	chia nhỏ thành các phần	分取された
Aliquoting	विभाज्य बनाना	teraliquot, tercuplik		分取
ANALYTE	विश्लेष्य पदार्थ	analit	chất phân tích	分析対象物質
ANONYMIZATION	गुमनाम करने	penghilangan identitas	ần danh	匿名化
ANONYMOUS	वेनाम,गुमनाम	tanpa identitas	vô danh	匿名
ASSENT	मंज़ूरी, सहमत	persetujuan	đồng ý, thừa nhận	アセント
associated data	संबद्ध डेटा	data terasosiasi, data terkait	dữ liệu liên quan	関連データ
AUDIT	लेखापरीक्षा करना	audit	kiểm toán, kiểm tra	監査
authentication	प्रमाणीकरण	autentikasi	xác thực	認証
AUTOPSY	शव-परीक्षा	autopsi	khám nghiệm từ thi	オートプシー
AXENIC STATE	असंदूषित अवस्था		trạng thái axenic (trạng thái thuần)	無菌状態

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Yadav, Birendra Kumar, et al. Biopreserv Biobank 20.3 (2022): 260-270.

ASEAN Feasibility Study Core Team





Clinical Microbiologist Clarity Labsolutions

Director, Laboratory Biorisk Consultancy & Training (LBCT) / On-Site Main Technical Expert to EU CBRN CoE Regional Secretariat - SEA

Head, Laboratory Research Division Research Institute for Tropical Medicine

Programme Director, National Implementation at the Verification Research, Training and Information Centre (VERTIC)

Associate Professor & Associate Dean **Duke-National University of Singapore** NUS - Medical School

meosc

OPEN SCIENCE

An approach to the scientific process that focuses on spreading knowledge as soon as it is available using digital and collaborative technology.

Open Science is a **policy priority for the European Commission** and the standard method of working under its research and innovation funding programmes as it improves the **quality, efficiency and responsiveness of research**.

Why?

When researchers share knowledge and data as early as possible in the research process with the relevant actors it helps diffuse the latest knowledge.





EOSC is a data infrastructure and could be seen as a twin approach to the pan-EU infrastructure organizations.

The latter offer the store, compute and connect services used by EOSC to offer the servicing of data and creating interoperability.

The combination forms the EOSC-ecosystem.





meosc

Aims to enable multidisciplinary discovery and use



Academic clinical laboratories are direct and/or indirect contributors of the EU research ecosystem.





meosc

Tripartite collaborations





neosc

Tripartite collaboration events





meosc

EOSC actors working with countries





meosc | cancer

1 September 2022 – 28 February 2025, ~8mEUR

To serve the European Cancer Mission,

via the engagement with large international coalitions: ICGC-Argo, GA4GH, 1+MG/B1MG, Cancer Core Europe, European Cancer Information System, European Network of Cancer Registries, Innovative Partnership for Action Against Cancer Joint Action, UNCAN.eu and patients/survivors associations

Academic clinical laboratories are direct and/or indirect contributors of the EU research ecosystem.









Is precision medicine implementation LMIC-friendly?



Comparison of CT accessibility in low-, middle-, and high-income countries.

- Artificial intelligence (AI) introduction in low- and middle-income countries (LMICs) should proceed differently than in high-income countries.
- Large differences in personnel, clinical experience, disease patterns, demographics, digital infrastructure, and radiology equipment dictate the need for a global health radiology AI strategy.
 - A comprehensive model for AI adoption in LMICs integrates clinical education, infrastructure deployment, and phased AI introduction.

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Mollura, Daniel J., et al. "Artificial intelligence in low-and middle-income countries: innovating global health radiology." Radiology 297.3 (2020): 513-520.

Looking into the future



Turning research output into an educational resource





Future challenges – increased complexity



Future challenges – increased complexity of research



Wolf SM. 2013. Annu. Rev. Genomics Hum. Genet. 14:557–77



The new normal in laboratory medicine

- Consolidation, economics of scale
- More services remotely, more often
- Information sharing, translating, integrating
- Accounting for complexity
- New technologies, new professions

- Jazieh AR, Kozlakidis Z. Healthcare transformation in the post-coronavirus pandemic era. Frontiers in Medicine. 2020 Jul 28;7:429.
- Kozlakidis Z, et al. Global health and data-driven policies for emergency responses to infectious disease outbreaks. The Lancet Global Health. 2020 Aug 10.









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THANK YOU

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