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EVALUATION REPORT OF THE IARC MEDIUM-TERM STRATEGY (MTS) 2021–2025 - APPENDICES

Evaluation of the International Agency for Research on Cancer (IARC) Medium-Term Strategy (MTS) 2021–2025

Appendices

Draft (20 March 2025)

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Bibliometric analysis

Context and objectives of the bibliometric analysis

This bibliometric analysis focuses on IARC's scientific production of IARC from January 2021 until April or May 2024[1]. It is part of the evaluation of the IARC MTS 2021–2025. It gives a synthesized overview of IARC's publications during the MTS period, and it provides some comparison with the previous MTS 2016–2020. The elements were discussed with the IARC Senior Advisory Team (SAT) of IARC during an SAT meeting on 6 June 2024 and with the Agency's management for the MTS retreat on 4 September 2024. This bibliometric analysis relies mainly on the evaluation framework and the KPIs of the MTS 2021–2025. This bibliometric analysis is an important contribution to the evaluation of the MTS 2021–2025 taking place in 2024. It corresponds with the following elements on publications of the MTS evaluation framework:

	Main ambitions of the MTS	Main indicators	Key performance indicators
Publications (Source: PLW)	✓ Promotion of scientific excellence in cancer prevention ✓ Collaborations between disciplines ✓ Implementation research	▪ SWOT analysis of the 5-year Branch Reviews ▪ Evaluation of IARC's contribution in the form of publications, taking into account the DORA and Leiden guidelines ▪ Manuscripts based on IARC grants per funder ▪ List of key publications per Pillar and selection of the 5 most relevant per Pillar, including comments on their scientific, public health, and societal impacts	• **Number and evolution of publications** • **Number and evolution of publications per scientific staff and ECVS** • **h-index overall and per Pillar**

Sources and methodology of the bibliometric analysis

The data presented in this bibliometric analysis were produced by IARC Publishing, Library and Web services (PLW) unit, in coordination with the Office of the Director. This analysis focuses on external journal articles; and chapters and books are considered out of scope. These bibliometric indicators are drawn from two major sources of data:

- **IARC's EndNote™ database** of external journal articles authored by IARC scientific staff. The records are imported from PubMed and Clarivate Web of Science™, and enhanced with custom coding of metadata, namely IARC Branch.
- **Clarivate Web of Science™**. The search parameters in Web of Science are: Science Citation Index and Emerging Sources Index, i.e. 2 files within the Web of Science platform; OG (organization enhanced name field)=International Agency for Research on Cancer(IARC). The FPY (final publication year) field is used to unambiguously identify publication dates.

It is worth mentioning that small discrepancies in the number of records between IARC's EndNote database and Web of Science may occur for several reasons (e.g. the affiliation name variants for IARC within Web of Science, the time required to manually code EndNote records with IARC Branches, records available in PubMed and not Web of Science, update of Web of Science). However, these minor differences between the two sources of data have a limited impact on the overall bibliometric analysis.

[1] Please note that in the MTS 2021–2025 Evaluation Report, certain indicators have been updated to include data for the full year 2024, where available. The data presented in the annex reflects the information received as of April 2024.

Bibliometric analysis of IARC publications

Corporate indicators

➔ Evolution of IARC's scientific publications

Table 1 presents the evolution of IARC's publications since 2016 with the proportion of peer-reviewed articles per year. After a regular increase during the previous MTS 2016–2020, the annual number of publications has been decreasing since the 2020 record of 470 publications but has remained higher than during the previous MTS. This downward trend aligns with global publication patterns observed by Clarivate Analytics. Notably, the proportion of peer-reviewed articles has remained consistently high and stable, ranging from 78% to 82% throughout the MTS 2021–2025 period.

Table 1. Number and evolution of IARC publications since 2016[2]

	Year	Articles	Peer-reviewed articles	% of peer-reviewed articles
MTS 2016–2020	2016	341	290	85%
	2017	352	291	83%
	2018	351	284	81%
	2019	371	292	78%
	2020	470	387	82%
MTS 2021–2025	2021	438	361	82%
	2022	440	341	78%
	2023	386	303	78%
	Apr 2024	101	83	82%

➔ Corporate h-index of IARC's scientific publications

The h-index is a KPI requested by IARC governance to represent the citation impact for the publications of a scientist or of a group of scientists (corporate h-index). The h-index is "defined as the number of papers with citation number ≥ *h*" [3]. For example, an h-index of 17 means that the scientist (or group of scientists) has published at least 17 papers, with each of these papers cited at least 17 times. As a signer of the San Francisco Declaration on Research Assessment (DORA), IARC is well aware of the benefits and the limitations of the h-index. Therefore, to complement the h-index, the Agency uses some qualitative indicators for the MTS evaluation, such as case studies. Table 2 presents IARC corporate h-index of IARC for the current and previous MTS periods. IARC's corporate h-index for January 2021–April 2024 is 63 for 1 365 publications. Because the h-index is a cumulative indicator, the oldest MTS periods logically have the highest h-indexes. In other words, the h-index KPI is useful for internal or external comparison, rather than a historical comparison.

Table 2. IARC corporate h-index of IARC for current and previous MTS periods[4]

Period	Total number of publications	Corporate h-Index
MTS 2005–2009 (5 years)	1 487	173
MTS 2010–2015 (6 years)	2 037	170
MTS 2016–2020 (5 years)	1 930	146
Current MTS 2021–2025 (3.33 years)	1 365	63

[2] Source: IARC-PLW, May 2024

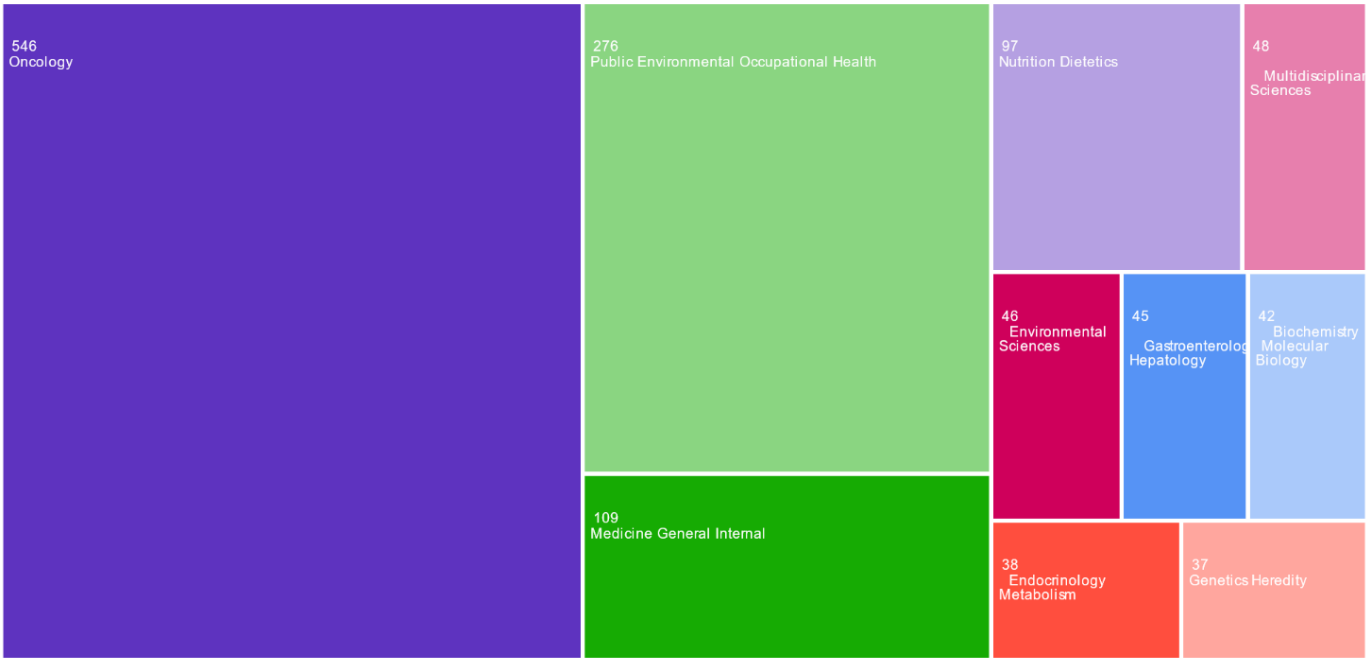
[3] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1283832/

[4] Source: IARC PLW, May 2024

In addition to the h-index, it is worth mentioning the scientific influence of IARC publications for 2021–May 2024 based on the Relative Citation Ratio (RCR). The RCR measures the scientific influence of each paper by field- and time-adjusting the citations it has received, and benchmarking to the median for United States National Institutes of Health (NIH) publications. This indicator shows that IARC's 1 341 publications for the period 2021–May 2024 are cited on average 12.39 times as much as similar articles in the same field for the same period.

➔ Topics of IARC's scientific publications

The chart below[5] shows IARC's scientific publications per topic for January 2021 until April 2024, according to the Web of Science™ categories. The main topics of IARC's scientific production are "Oncology" (all Pillars), followed by "Public environmental and occupational health" (Pillar 3).



➔ Scientific productivity of IARC's scientists (January 2021–April 2024)

In accordance with the MTS evaluation framework, the number and evolution of publications is presented per scientific staff (P staff) members and Early Career and Visiting Scientist (ECVS), showing the scientific productivity of the Agency. The table below shows the productivity of the IARC scientific personnel from January 2021 to April 2024. P staff members correspond to the statutory Scientists, and the ECVSs are mainly doctoral students and postdoctoral scientists.

On average, 1.85 publications were published per year for each IARC scientific personnel (P staff and ECVS) during the first 3 years of the MTS period. This ratio goes up to 4.58 publications per year for each P staff member. Restricting to scientific P staff, the average number of publications reaches **6 publications per year for each P staff member in the Branches.**

These ratios tend to increase compared with the previous MTS period, demonstrating an improvement in productivity of IARC scientific personnel. The year 2024 is not taken into consideration, because the information on publications for the whole year 2024 is not yet available.

[5] Source: Web of Science™, May 2024

Table 3. Number of publications for IARC scientific personnel[6]

MTS	Year	Publica-tions	P Staff	Number of publications per P staff	ECVS	Number of publications per ECVS	Total scientific staff	Number of publications per scientific staff (P staff and ECVS)
MTS 2016–2020	2016	341	103	3.31	99	3.44	202	1.68
	2017	352	106	3.32	104	3.38	210	1.67
	2018	351	102	3.44	118	2.97	220	1.59
	2019	371	106	3.50	109	3.40	215	1.72
	2020	470	103	4.56	126	3.73	229	2.05
MTS 2021–2025	2021	438	99	4.42	115	3.81	214	2.05
	2022	440	87	5.06	147	2.99	234	1.88
	2023	386	90	4.29	132	2.92	222	1.74
	April 2024	101	98	–	145	–	243	–

➔ Benchmarking IARC's publication impact amongst leading cancer research institutions

Table 4 compares IARC's publication impact from 2021 to October 2024 with that of prominent cancer research institutions across France, Europe, the USA, and other countries. Key metrics include the number of publications, total citations, average citations per publication, and the corporate H-index, providing insight into the reach and influence of each institution's research output.

While IARC's publication volume is modest due to its smaller size compared to other leading cancer institutions, it is substantial relative to its capacity. Notably, IARC's citations-per-publication ratio is **2 to 6 times higher than other leading institutions in oncology**, underscoring the high impact and relevance of its research. Additionally, IARC's corporate H-index is relatively high, highlighting IARC's role as a major contributor to impactful cancer research.

[6] Source: IARC-PLW, HRO and LCB, Web of Science™, April 2024

Benchmarks	Institutions	Publications for IARC (2021-October 2024)			
		Number of publications	Number of citations	Average citations per publications	Corporate H-index
	IARC – WHO (Lyon – France)	1219	73610	60,39	59
France	CLB – CRCL (Lyon – France)	1032	15431 14,95	14,95	52
	Institut Curie (Paris – France)	1191	14600	12,26	51
	Institut Gustave Roussy (Paris Villejuif – France)	1833	35942	19,23	83
Europe	Trinity College (Dublin – Ireland)	307	5003	16,3	28
	Imperial College (London – UK)	944	15628	16,56	50
	Erasmus MC (Rotterdam – Netherlands)	1784	24662	13,82	62
	Karolinska Inst. (Stockholm – Sweden)	1751	19960	11,4	57
USA	Stanford Cancer Institute (Palo Alto – USA)	423	13900	32,86	54
	Fred Hutchinson Cancer Center (Seattle – USA)	1391	27391	19,69	73
	St. Jude Children's Research Hospital (Memphis – USA)	993	12666	12,76	52
	Moffitt Cancer Center (Tampa – USA)	1613	31362	19,44	76
	Mayo Clinic (USA)	3134	43993	14,04	83
	Harvard (Cambridge – Boston – USA)	7055	111751	15,84	130
	MD Anderson (Houston – USA)	5068	81384	16,06	119
Other countries	MC Gill University (Montreal – Canada)	939	10425	11,1	47
	University of Toronto (Toronto – Canada)	3306	40005	12,1	81
	Fudan University (Shanghai – China)	3814	36960	9,69	68
	University of Sydney (Sydney – Australia)	1428	19916	13,95	59

Detailed indicators

➔ IARC publications by Pillars and Branches

shows the distribution of IARC publications according to IARC's Pillars and Branches, from January 2021 until May 2024. The total number of articles coded by Branch for this period was 1419. Articles published by more than one Branch (100 publications) are counted more than once in this table. Pillar 2 accounts for half of IARC's publications, and the Nutrition and Metabolism Branch (NME) accounts for nearly one third of the production of the Agency. Publications related to the European Prospective Investigation into Cancer and Nutrition (EPIC) contribute 9% of IARC's articles. It is worth noting that co-publications across IARC Branches (with at least 2 co-authors from 2 separate Branches) represent only 7% of IARC scientific production for the period January 2021 until April 2024.

Table 5. IARC scientific publications by Pillar and Branch, January 2021 to April 2024[7]

	Pillar 1	Pillar 2			Pillar 3			Pillar 4
Year / Branch	CSU	GEM	NME	LSB	ENV	EGM	EPR	ESC
2021	71	82	143	13	49	22	69	23
2022	78	68	113	35	40	29	75	40
2023	62	69	123	14	48	24	70	38
April 2024	13	24	32	1	12	8	23	8
Totals by Branch	224	243	411	63	149	83	237	109
Totals by Pillar	224		717			469		109
% by Pillar	16%		51%			33%		8%

Table 6 presents the distribution of IARC publications and the h-index per Branch, for the period January 2021–April 2024 (the h-index is defined in 2.1). CSU is the Branch with the highest cumulative h-index, at 36 for the observed period and a total of 218 publications, followed by NME with an h-index of 30 and a total of 407 publications.

Table 6. Scientific publications and h-index by Branch, January 2021 to April 2024[8]

Pillar	Branches	Number of publications	h-Index
Pillar 1	CSU	218	36
Pillar 2	GEM	234	24
	NME	407	30
	LSB	52	11
Pillar 3	ENV	148	16
	EGM	80	12
	EPR	229	24
Pillar 4	ESC	106	20
Total	IARC	1 324	62

[7] Source: IARC-PLW, May 2024

[8] Source: *Ibid.*

Table 7 presents the distribution of IARC publications and the h-index per Pillar, for the period January 2021–April 2024. Pillars 1 and 2 have the highest h-index.

Table 7. Scientific publications and h-index by Pillar, January 2021 to April 2024.[9]

Pillar	Number of publications	h-index for period
Pillar 1	218	36
Pillar 2	653	38
Pillar 3	440	28
Pillar 4	106	20
Total	**1 324**	**62**

Table 8 presents the distribution of IARC publications and the RCR index per Branch, for the period January 2021–May 2024 (RCR is defined in 2.1). CSU is the Branch with the highest RCR; CSU publications are cited on average 52.39 times as much as other publications in the same field, and ESC publications 12.05 times as much.

Scientific publications and RCR index by Branch, January 2021 to May 2024.[10]

Pillars	Branches	Number of publications	RCR-index
Pillar 1	CSU	222	52.38
Pillar 2	GEM	241	3.77
	NME	408	3.67
	LSB	51	3.18
Pillar 3	ENV	147	1.95
	EGM	82	1.5
	EPR	236	3.2
Pillar 4	ESC	107	12.05
Total	IARC	1 341	12.39

Table 9 presents the distribution of IARC publications and the RCR index per Pillar, for the current MTS period. As observed above, Pillars 1 and 4 have the highest RCR index for the observed period, with a RCR of 52.38 and a total of 222 publications for Pillar 1, followed by a RCR of 12.05 and a total of 107 publications for Pillar 4.

Scientific publications and RCR index by Pillar, January 2021 to May 2024[11]

Pillar	Number of publications	RCR-index
Pillar 1	222	52.38
Pillar 2	659	3.41
Pillar 3	447	2.57
Pillar 4	107	12.05
Total	**1 341**	**12.39**

[9] Source: *Ibid.*
[10] Source: IARC-PLW, June 2024
[11] Source: IARC-PLW, June 2024.

➔ Scientific productivity within the Branches

Table 10 shows the scientific productivity within IARC Branches for January 2021 to April 2024. It presents the ratio between the number of publications per Branch and the average number of scientific personnel (P staff and ECVS) for this same period. The three Branches of IARC with the highest scientific productivity for the MTS period January 2021 until April 2024, as measured by the average number of articles per personnel member, are NME, CSU, and GEM. On average across the Agency each scientific staff member of IARC produced 6.5 publications during this period.

Table 10. Number of publications according to the type of personnel.[12]

Branch	Publications January 2021 to April 2024	Number of P staff (PI)	Articles per P-staff	Number of ECVS	Articles per ECVS	Total personnel (P staff and ECVS)	Articles per scientific personnel
CSU	218	9.5	22.9	17.5	12.5	27	8.1
GEM	234	12.0	19.5	18.5	12.6	30.5	7.7
NME	407	12.0	33.9	33.3	12.2	45.3	9.0
ENV	148	7.3	20.3	17.0	8.7	24.3	6.1
EGM	80	5.8	13.8	13.0	6.2	18.8	4.3
EPR	229	13.5	17.0	23.8	9.6	37.3	6.1
ESC	106	11.3	9.4	7.8	13.6	19.1	5.5
IARC	**1324**	**71.4**	**18.5**	**130.9**	**10.1**	**202.3**	**6.5**

➔ The publications of IARC related to the main funders

The top 7 funders of IARC represent 78% of the external budget of the Agency for 2021–2023, to support IARC's scientific programmes. Those funding agencies or foundations are the European Commission (EC) and institutions in the USA (National Institutes of Health [NIH], Bill & Melinda Gates Foundation [BMGF]), in France (French National Cancer Institute [INCa]), and in the United Kingdom (Medical Research Council [MRC], World Cancer Research Fund [WCRF], Cancer Research UK [CRUK]). From January 2021 to April 2024, 83% of IARC publications are associated with the top 7 funders of the Agency.

Table 11. Number of IARC publications by funder January 2021 to April 2024[13]

Main Funders	2021	2022	2023	April 2024	Total
EC (BE)	71	66	35	10	182
NIH (USA)	85	81	72	23	261
INCA (FR)	33	20	29	8	90
MRC (UK)	90	74	50	8	222
BMGF (USA)	9	6	5	1	21
WCRF (UK)	54	53	36	8	151
CRUK (UK)	76	68	51	10	205
Total (%) for Top 7 funders	418 (95%)	368 (84%)	278 (72%)	68 (67%)	1 132 (83%)
Total	**438**	**440**	**386**	**101**	**1365**

[12] Source: IARC-PLW, HRO and LCB, Web of Science™, May 2024

[13] Source: IARC-PLW and RMO, May 2024

➔ IARC publications related to the WHO global initiatives on cancer

Table 12 details the number and proportion of publications related to the 3 WHO global cancer initiatives (on childhood cancer, cervical cancer, and breast cancer) for January 2021 until November 2023.

Table 12. Number and evolution of the publications of IARC related to the WHO global initiatives on cancer since 2021[14]

	2021	2022	2023	Nov. 2024
WHO Global Breast Cancer Initiative (IARC Branches : CSU, EPR, ENV, ESC)	23 IARC publications on breast cancer 8 publications related to the WHO Global Breast Cancer Initiative (35%)	22 IARC publications on breast cancer 10 publications related to the WHO Global Breast Cancer Initiative (45%)	36 IARC publications on breast cancer 19 publications related to the WHO Global Breast Cancer Initiative (53%)	21 IARC publications on breast cancer 11 publications related to the WHO Global Breast Cancer Initiative (52%)
WHO Cervical Cancer Elimination Initiative (IARC Branches: CSU, EPR, ESC)	10 IARC publications on cervical cancer 9 publications related to the WHO Cervical Cancer Elimination Initiative (90%)	14 IARC publications on cervical cancer 14 publications related to the WHO Cervical Cancer Elimination Initiative (100%)	30 IARC publications on cervical cancer 28 publications related to the WHO Cervical Cancer Elimination Initiative (93%)	13 IARC publications on cervical cancer 13 publications related to the WHO Cervical Cancer Elimination Initiative (100%)
WHO Global Initiative for Childhood Cancer (GICC) (IARC Branches : CSU, ENV, ESC)	6 IARC publications on childhood cancer 3 publications related to the WHO Global Initiative for Childhood Cancer (50%)	10 IARC publications on childhood cancer 5 related to the WHO Global Initiative for Childhood Cancer (50%)	7 IARC publications on childhood cancer 4 publications related to the WHO Global Initiative for Childhood Cancer (57%)	7 IARC publications on childhood cancer 5 publications related to the WHO Global Initiative for Childhood Cancer (71%)

➔ The publications with international collaborations

Table 13 displays the number and proportion of international collaborations in IARC publications. These figures were produced by analysing the percentage of IARC publications whose co-author affiliations include addresses in more than one country. Of the total of 1365 papers published by IARC from January 2021 to April 2024, 1320 publications (97%) involved international collaboration,

[14] Source: IARC, DIR Office and SSR (PLW), November 2024

including a co-author affiliation from at least one other country. This percentage is slightly higher than the proportion for the previous MTS 2016–2020 (93%).

Table 13. Number and proportion of IARC publications with international collaborations January 2021 to April 2024.[15]

	2021	2022	2023	April 2024	Total
Number of publications	426 of 438	423 of 440	372 of 386	99 of 101	1320 of 1365
% of publications	97%	96%	96%	98%	97%

Table 14 presents the top 50 countries co-publishing with IARC from January 2021 until April 2024. Scientific institutions in European countries as well as the USA and Australia are the main partners for IARC international co-publications. Within the top 25 countries for IARC co-publications, 22 are IARC Participating States; the 3 exceptions are Greece, Colombia, and South Africa.

Table 14. Top 50 countries for IARC co-publications in January 2021 to April 2024.[16]

Row	Country	Publications	%	Row	Country	Publications	%
1	UK	684	51.82%	26	CZECHIA	59	4.47%
2	USA	637	48.26%	27	SINGAPORE	54	4.09%
3	GERMANY	408	30.91%	28	ISRAEL	52	3.94%
4	ITALY	359	27.20%	29	MEXICO	47	3.56%
5	SPAIN	341	25.83%	30	NEW ZEALAND	44	3.33%
6	SWEDEN	294	22.27%	31	PORTUGAL	43	3.26%
7	NETHERLANDS	293	22.20%	32	RUSSIAN FED.	43	3.26%
8	FRANCE	276	20.91%	33	REP. OF KOREA	41	3.11%
9	NORWAY	248	18.79%	34	POLAND	40	3.03%
10	AUSTRALIA	243	18.41%	35	HUNGARY	38	2.88%
11	CANADA	237	17.96%	36	KENYA	37	2.80%
12	DENMARK	236	17.88%	37	MALAYSIA	37	2.80%
13	CHINA	135	10.23%	38	UGANDA	36	2.73%
14	GREECE	127	9.62%	39	COSTA RICA	33	2.50%
15	SWITZERLAND	117	8.86%	40	ARGENTINA	30	2.27%
16	BELGIUM	105	7.96%	41	NIGERIA	30	2.27%
17	AUSTRIA	95	7.20%	42	ZIMBABWE	29	2.20%
18	BRAZIL	95	7.20%	43	MOROCCO	26	1.97%
19	FINLAND	86	6.52%	44	COTE D'IVOIRE	24	1.82%
20	JAPAN	86	6.52%	45	SAUDI ARABIA	24	1.82%
21	COLOMBIA	84	6.36%	46	INDONESIA	23	1.74%
22	INDIA	77	5.83%	47	ROMANIA	23	1.74%
23	IRAN (ISLAMIC REPUBLIC OF)	65	4.92%	48	CHILE	21	1.59%
24	IRELAND	60	4.55%	49	CYPRUS	21	1.59%
25	SOUTH AFRICA	60	4.55%	50	MALAWI	21	1.59%

[15] Source: IARC-PLW, May 2024

[16] Source: *ibid.*

Table 15 shows the top 50 institutions for IARC co-publications from January 2021 until April 2024.

Table 15. Top 50 institutions for IARC co-publications in January 2021 to April 2024.

	Institution	Publications	%		Institution	Publications	%
1	HELMHOLTZ ASSOCIATION	263	19.92%	26	FRED HUTCHINSON CANCER CENTER	120	9.09 %
2	NATIONAL INSTITUTES OF HEALTH NIH USA	254	19.24%	27	UTRECHT UNIVERSITY	117	8.86 %
3	GERMAN CANCER RESEARCH CENTER DKFZ	241	18.26%	28	HARVARD MEDICAL SCHOOL	114	8.64 %
4	IMPERIAL COLLEGE LONDON	239	18.11%	29	UIT THE ARCTIC UNIVERSITY OF TROMSØ	114	8.64 %
5	NIH NATIONAL CANCER INSTITUTE NCI	238	18.03%	30	UNIVERSITY OF CALIFORNIA SYSTEM	112	8.49 %
6	CIBER CENTRO DE INVESTIGACION BIOMEDICA EN RED	234	17.73%	31	INSTITUTO DE INVESTIGACION BIOSANITARIA IBS GRANADA	110	8.33 %
7	INSERM	202	15.30%	32	UNIVERSITY OF POTSDAM	106	8.03 %
8	CIBERESP	200	15.15%	33	ESCUELA ANDALUZA DE SALUD PUBLICA	104	7.88 %
9	HARVARD UNIVERSITY	189	14.32%	34	HOSPITAL CLINICO UNIVERSITARIO VIRGEN DE LA ARRIXACA	103	7.80 %
10	UNIVERSITY OF OXFORD	180	13.64%	35	LUND UNIVERSITY	100	7.58 %
11	UNIVERSITE PARIS CITE	172	13.03%	36	PUBLIC HEALTH INSTITUTE OF NAVARRA	100	7.58 %
12	UNIVERSITY OF LONDON	171	12.96%	37	UNIVERSITY OF MELBOURNE	100	7.58 %
13	INSTITUT CATALA D ONCOLOGIA	167	12.65%	38	MELBOURNE GENOMICS HEALTH ALLIANCE	99	7.50 %
14	UMEA UNIVERSITY	167	12.65%	39	AARHUS UNIVERSITY	98	7.42 %

15	DANISH CANCER SOCIETY	156	11.82%	40	GUSTAVE ROUSSY	94	7.12%
16	INSTITUT D INVESTIGACIO BIOMEDICA DE BELLVITGE IDIBELL	153	11.59%	41	BRIGHAM WOMEN S HOSPITAL	92	6.97 %
17	HARVARD T H CHAN SCHOOL OF PUBLIC HEALTH	151	11.44%	42	UNIVERSITY OF GRANADA	86	6.52 %
18	UNIVERSITY OF TORONTO	148	11.21%	43	UNIVERSITY OF TURIN	85	6.44 %
19	UNIVERSITÉ PARIS SACLAY	135	10.23%	44	UNIVERSITY OF WASHINGTO N	84	6.36 %
20	UNIVERSITY OF COPENHAGEN	135	10.23%	45	UNIVERSITY OF WASHINGTO N SEATTLE	84	6.36 %
21	UNICANCER	131	9.92%	46	AMERICAN CANCER SOCIETY	83	6.29 %
22	DEUTSCHES INSTITUT FÜR ERNAHRUNGSF ORSCHUNG POTSDAM	127	9.62%	47	LUNENFELD TANENBAUM RESEARCH INSTITUTE	83	6.29 %
23	FONDAZIONE IRCCS ISTITUTO NAZIONALE TUMORI MILAN	124	9.39%	48	SINAI HEALTH SYSTEM TORONTO	83	6.29 %
24	KAROLINSKA INSTITUTET	123	9.32%	49	UNIVERSITY OF TEXAS SYSTEM	83	6.29 %
25	UNIVERSITY OF OSLO	122	9.24%	50	UTRECHT UNIVERSITY MEDICAL CENTER	83	6.29 %

Key publications per Pillar

As defined in the MTS evaluation framework, the Pillar coordinators have each selected 5 or 6 publications for the 2021–2024 period. These publications are representative of the Pillar's scientific activities and contribution to the implementation of the MTS 2021–2025.

➔ Pillar 1 – Data for action

Publication #1:

Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries
Authors: Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A
References: CA: *A Cancer Journal for Clinicians*; Volume: 74, Issue: 3, Pages: 229-263; April 4, 2024

Summary
This publication presents global cancer statistics for 2022, emphasizing geographical variability across 20 world regions in the 10 leading cancer types. It discusses recent trends and underlying determinants, highlighting the importance of investments in prevention: "the targeting of key risk factors for cancer (including smoking, overweight and obesity, and infection) could avert millions of future cancer diagnoses and save many lives worldwide, bringing huge economic as well as societal dividends to countries over the forthcoming decades."

Scientific, public health, and societal impacts
This paper serves as a key reference for global and regional cancer burden estimates from IARC and provides an overview of evidence for cancer prevention worldwide. Given that CA is the flagship journal of the ACS (IF_{2023}=503), citations are expected to align with previous estimates from 2018 and 2020, which were each received around 50,000 to 60,000 citations. The GCO offers country estimates (from other IARC flagship publications (e.g. CI5-XII) and programmes (e.g. GICR) from Pillar I) in various format., which have attracted 9.2 million page views and 731,000 users for February to August 2024. The GLOBOCAN database has been widely shared with WHO and other key partners.

Contribution to the MTS implementation
IARC aims to "disseminate flagship databases such as GLOBOCAN via the Global Cancer Observatory (GCO) in a timely manner. The cancer surveillance data collected by cancer registries will remain the basis for the national indicators, which will facilitate cancer planning and prioritization globally and help individual countries in determining changes in the scale and profile of cancer, the role of specific risk factors, and the impact of interventions" (refer to "Implementing the MTS 2021–2025", IARC MTS 2021–2025, p. 31).

Publication #2:

Cancer survival in Africa, central and south America, and Asia (SURVCAN-3): a population-based benchmarking study in 32 countries
Authors: Soerjomataram I, Cabasag C, Bardot A, Fidler-Benaoudia MM, Miranda-Filho A, Ferlay J, Parkin DM, Ranganathan R, Piñeros M, Znaor A, Mery L, Joko-Fru YW, Dikshit R, Sankaranarayanan R, Swaminathan R, Bray F; SURVCAN-3 collaborators
References: Lancet Oncology; Volume: 24, Issue: 1, Pages 22-32; January 24, 2023

Summary
Cancer survival is a key measure of the overall effectiveness of the health system in delivering cancer care; however, the availability and quality of the statistics remain limited in transitioning countries. SURVCAN-3 analyses net survival for 15 cancer types using data from 68 registries and identifies three groups based on outcomes and Human Development Index (HDI):

- Low survival (< 30%): cancers such as lung and stomach, with minimal HDI variation.
- Intermediate survival (30–79%): cancers such as cervix and colorectum, showing moderate HDI variation.
- High survival (≥ 80%): cancers such as breast and prostate, showing substantial HDI variation.

Scientific, public health, and societal impacts
Undertaken with multidisciplinary teams worldwide, IARC flagship programmes on cancer survival, SurvMark and SURVCAN, aim to redefine benchmarking studies through reliable survival statistics across income levels. As well as benchmarking survival estimates in countries in transition, SURVCAN-3 aims to enhance local registry expertise in data collection and survival analysis, aligning with IARC and GICR initiatives to assist registries to improve data practices and support future research.

Contribution to the MTS implementation
"The capturing and benchmarking of cancer outcomes internationally will continue. Activities include the provision of high-quality survival indicators through bilateral collaboration to increase local capacity and ensure complete follow-up (SURVCAN)" (refer to "Implementing the MTS 2021–2025", IARC MTS 2021–2025, p. 7).

Publication #3:

Global Stage Distribution of Breast Cancer at Diagnosis: A Systematic Review and Meta Analysis
Authors: Benitez Fuentes JD, Morgan E, de Luna Aguilar A, Mafra A, Shah R, Giusti F, Vignat J, Znaor A, Musetti C, Yip CH, Van Eycken L, Jedy-Agba E, Piñeros M, Soerjomataram I
References: *JAMA Oncology;* Volume:10, Issue: 1, Pages: 7-15; 2024

Summary
Stage is an important indicator for awareness of breast cancer and effectiveness of early detection and screening programmes. This systematic review and meta-analysis examined the global distribution of breast cancer stage at diagnosis, using registry data from 81 countries. The study highlights significant disparities; the proportion of cases presenting with distant metastatic breast cancer is particularly high in sub-Saharan Africa (5.6–30.6%) compared with North America (0.0–6.0%). In high-income countries with historical data, a decrease or stabilization in distant metastatic diagnoses was observed. Key factors influencing these trends included older age and lower socioeconomic status.

Scientific, public health, and societal impacts
This research marks the first global reporting of breast cancer stage data. It reveals ongoing inequalities within and among countries and advocates for heightened awareness of breast cancer symptoms and the importance of early detection. The study also identifies a lack of high-quality data, suggesting the importance of improving global coverage and the quality of population-based cancer registries. This research is aligned with IARC's mission to provide evidence for cancer prevention and improve cancer registry capacity.

Contribution to the MTS implementation
The findings contribute to the MTS as a global reference for cancer indicators (refer to "Implementing the MTS 2021–2025", IARC MTS 2021–2025, p. 7), providing the baseline data needed to monitor and evaluate screening programmes (Ibid., p. 8). In addition, they underscore the need for improved coverage, quality, and networking capabilities of cancer registries worldwide (Ibid., p. 7).

Publication #4:

Quantitative estimates of preventable and treatable deaths from 36 cancers worldwide: a population-based study
Authors: Frick C, Rumgay H, Vignat J, Ginsburg O, Nolte E, Bray F, Soerjomataram I
References: The Lancet Global Health; Volume: 11, Issue: 10, Pages: e1444-e1454; September 26, 2023

Summary
Cancer is a leading cause of premature mortality worldwide. This study estimates premature deaths among individuals aged 30–69 years, distinguishing between deaths that are preventable (via primary or secondary prevention) and those that are treatable (via curative treatment). In 2020, there were 182.8 million years of life lost (YLLs) due to premature cancer deaths, with 124.3 million (68.0%) classified as preventable and 58.5 million (32.0%) as treatable. Lung cancer accounted for the largest proportion of preventable premature YLLs in countries with medium to very high HDI (17.4% of all cancers), and cervical cancer was the leading cause in countries with low HDI (26.3% of all preventable cancers). Colorectal and breast cancers emerged as significant treatable cancers across all HDI tiers (25·5% of all treatable cancers combined).

Scientific, public health, and societal impacts
This study highlights the varying impact of specific cancer types on premature death across countries, levels of human development, and sexes. It provides the epidemiological framework for the recent Lancet Commission on women, power, and cancer. The novel metrics proposed advocate for increased investment in risk-factor reduction and vaccination to address premature cancer inequalities, as well as tailored programmes for early diagnosis and screening linked to timely and comprehensive treatment.

Contribution to the MTS implementation
The study aligns with IARC's goal of promoting "improved knowledge on cancer prevention", as outlined in the MTS 2021–2025. "As cancer profiles in LMICs increasingly resemble those in high-income countries, IARC enables reporting on relevant changes in the magnitude and distribution of relevant global indicators" (refer to "Implementing the MTS 2021–2025", IARC MTS 2021–2025, p. 31).

Publication #5:

Global burden of cancer in 2020 attributable to alcohol consumption: a population-based study
Authors: Rumgay H, Shield K, Charvat H, Ferrari P, Sornpaisarn B, Obot I, Islami F, Lemmens VEPP, Rehm J, Soerjomataram I
References: The Lancet Oncology; Volume: 22, Issue: 8, Pages: 1071-1080; August 2021

Summary
Alcohol use is causally linked to multiple cancers. This study quantifies the proportion of cancer cases attributable to alcohol consumption, revealing that approximately 741,300 cancers (4.1% of all cancers) were linked to alcohol use. Oesophageal, liver and breast cancers are the most significant contributors, with the highest burden observed in Eastern Asia and Central and Eastern Europe. Notably, while heavy drinking accounted for a considerable portion of new cancer cases, moderate drinking also contributed significantly.

Scientific, public health, and societal impacts
Despite a decline in alcohol consumption in many regions, including Europe, this study highlights alcohol's continued importance as a cancer risk factor. It emphasizes that there is no safe level of alcohol consumption for cancer prevention. These findings have informed multiple policy briefs by the WHO Regional Office for Europe and the European Union, supporting global alcohol control initiatives, particularly in Europe. In addition, the study has garnered attention from media, social societies, and clinical organizations.

Contribution to the MTS implementation
This study directly contributes to IARC's MTS by providing a global indicator of disease burden to support cancer prevention (refer to "Implementing the MTS 2021–2025", IARC MTS 2021–2025, p. 6). It also provides baseline information necessary for implementing primary prevention interventions targeting established, modifiable risk factors (Ibid., p. 7).

➔ **Pillar 2 – Understanding the causes of cancer**

Publication #1:

Lifestyle changes in middle age and risk of cancer: evidence from EPIC
Authors: P Ferrari, H Freisling, I Huybrechts, K Matta, E Weiderpass
References: European Journal of Epidemiology; Volume: 39, Pages: 147–159; January 5, 2024

Summary
This study evaluates the impact of changing lifestyle habits on cancer risk by comparing lifestyle assessments at baseline and during follow-up. A Healthy Lifestyle Index (HLI) score was calculated based on factors such as cigarette smoking, alcohol consumption, body mass index, and physical activity. Among participants in the top third of the HLI at baseline (considered healthy), those who fell to the bottom third at follow-up (considered unhealthy) had a 21% higher risk of lifestyle-related cancers (HR, 1.21; 95% CI, 1.07–1.37) compared with those who remained in the top third. Conversely, among participants considered unhealthy at baseline, those who improved to the top third at follow-up had a 25% lower risk of lifestyle-related cancers compared with those who remained in the bottom third.

Scientific, public health, and societal impacts
These findings indicate that lifestyle changes during adulthood can significantly influence cancer risk in both men and women. Favourable lifestyle modifications are associated with reduced cancer risk, while unfavourable changes correlate with increased risk. Policy-makers, clinicians, and general practitioners should emphasize the importance of even small lifestyle improvements in reducing cancer risk, when developing or advising adults and elderly people about health measures.

Contribution to the MTS implementation
This publication directly contributes to Pillar II of the MTS 2021–2025: "Understanding the causes of cancer" (refer to "Implementing the MTS 2021–2025", IARC MTS 2021–2025, p. 21).

Publication #2:

Consumption of ultra-processed foods and risk of multimorbidity of cancer and cardiometabolic diseases: a multinational cohort study
Authors: H Freisling, I Huybrechts, V Viallon, P Ferrari
References: Lancet Regional Health Europe; Volume: 14, Issue: 35; November 2023; Scientific, public health, and societal impacts
Summary
This study investigates the relationship between total and subgroup consumption of ultra-processed foods (UPFs) and the risk of multimorbidity, defined as the co-occurrence of at least two chronic diseases, including cancer at any site, cardiovascular disease, and type 2 diabetes. The results indicate that higher UPF consumption (excluding alcoholic beverages) is associated with an increased risk of multimorbidity related to cancer and cardiometabolic diseases (HR, 1.09; 95% CI, 1.05–1.12). These findings suggest that a greater intake of UPFs may increase the risk of developing multimorbidity involving cancer and cardiometabolic conditions.

Scientific, public health, and societal impacts
Multimorbidity represents a continuum, which starts when a previously healthy individual develops a chronic disease. The study highlights that higher consumption of ultra-processed foods (UPFs) before a first chronic condition may adversely affect disease prognosis by increasing the risk of multimorbidity. This is a growing health challenge not only in Europe but globally. The findings provide crucial evidence that can aid policy-makers in formulating lifestyle recommendations and interventions aimed at reducing UPF consumption and controlling cancer and multimorbidity.

Contribution to the MTS implementation
This publication directly contributes to Pillar II of the MTS 2021–2025: "Understanding the causes of cancer" (refer to "Implementing the MTS 2021–2025", IARC MTS 2021–2025, p. 21).

Publication #3:

Circulating inflammatory and immune response proteins and endometrial cancer risk: a nested case-control study and Mendelian randomization analyses
Authors: S Wang, V Viallon, M Lee, N Dimou, C Biessy, ..., S Rinaldi, M Gunter, L Dossus
References: Ebio Medicine; In press

Summary
This study explores the role of inflammation and immune dysregulation in endometrial carcinogenesis by measuring 152 plasma protein biomarkers pre-diagnostically in 624 endometrial cancer case–control pairs nested within the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort. Selected proteins associated with endometrial cancer risk were further analysed in a two-sample Mendelian randomization (MR) using data from the UK Biobank (n = 52 363) and the Endometrial Cancer Association Consortium (12 270 cases and 46 126 controls). In EPIC, IL-6 (OR, 1.28; 95% CI, 1.03–1.57) and HGF (1.48; 1.06–2.07) were positively associated with endometrial cancer risk, while HSD11B1 (0.67; 0.49–0.91), SCF (0.68; 0.49–0.94), and CCL25 (0.80; 0.65–0.99) showed inverse associations. MR analysis indicated IL-6 (OR, 1.19; 95% CI, 1.04–1.36) and HSD11B1 (0.91; 0.84–0.99) as associated with endometrial cancer risk.

Scientific, public health, and societal impacts
Using a combination of nested case–control and Mendelian randomization analyses, this study identifies circulating biomarkers that may reflect inflammation and immune response pathways associated with endometrial cancer risk. In particular, altered IL-6 signalling and reduced glucocorticoid activity via the HSD11B1 enzyme may play roles in endometrial carcinogenesis. These findings provide insights into the biological mechanisms connecting inflammation and immune response alterations to endometrial cancer. The study also underscores the potential of proteomics in investigating the etiology of rising cancer incidences, such as endometrial cancer.

Contribution to the MTS implementation
This publication directly contributes to Pillar II of the MTS 2021–2025: "Understanding the causes of cancer" (refer to "Implementing the MTS 2021–2025", IARC MTS 2021–2025, p. 21).

Publication #4:

Geographic variation of mutagenic exposures in kidney cancer genomes
Authors: Senkin S, Moody S, de Carvalho A, Perdomo S, Alexandrov LB, Stratton MR, Brennan P
References: Nature; Volume: 629 - Pages: 910-918; May 23, 2024

Summary
Although smoking, obesity, and hypertension are known causes of renal cancer, they do not explain the geographical variation in incidence rates. This study analysed DNA mutations in tumour samples (mutational signatures) from 962 renal cancer cases across 11 countries to identify potential unknown causes of the disease. The somatic mutation profiles varied between countries. Notably, the mutational signatures associated with aristolochic acid compounds were prevalent in Romania, Serbia, and Thailand, and rare in other regions. In Japan more than 70% of cases exhibited

a mutational signature of unknown origin, compared with less than 2% in other countries. In addition, a common mutational signature of unknown origin was found to have higher mutation loads in countries with higher kidney cancer incidence rates.

Scientific, public health, and societal impacts
The study identifies the existence of multiple, geographically variable, mutagenic exposures that may affect tens of millions of people and illustrates the potential for new insights into cancer causation through large-scale global cancer genomics.

Contribution to the MTS implementation
The study demonstrates widespread exposure to aristolochic acid, a known carcinogen, in certain parts of Europe and Southeast Asia, likely affecting millions of people. It also provides evidence of a mutagenic exposure prevalent in Japan and further identifies an additional mutagen that may account for the high risk of renal cancer in central Europe. This finding is crucial for public health initiatives aimed at reducing cancer risk in populations exposed to this harmful compound, thereby directly supporting IARC's Emerging Priority #1: "Evolving cancer risk factors and populations in transition" (refer to "Implementing the MTS 2021–2025", IARC MTS 2021–2025, p. 25).

Overall, this publication emphasizes the importance of global collaboration in cancer genomics research and reinforces IARC's comparative advantage: "Global scientific convening power and large collaborative research networks" (Ibid., p. 20).

Publication #5:

Blood proteome of imminent lung cancer diagnosis
Authors: The Lung Cancer Cohort Consortium, Lead team (GEM): Johansson M, Robbins H, Zahed H, Alcala K
References: Nature Communications; Volume: 24 – Article number: 3726; June 1, 2023

Summary
Identification of risk biomarkers may enhance early detection of smoking-related lung cancer. Within the framework of the US NCI-funded INTEGRAL project, the researchers measured between 392 and 1162 proteins in blood samples taken up to 3 years before diagnosis from 731 smoking-matched case–control sets nested within six prospective cohorts from the USA, Europe, Singapore, and Australia. The study identifies 36 proteins with independently reproducible associations with risk of imminent lung cancer diagnosis (all $P < 0.0005$).

Scientific, public health, and societal impacts
As lung cancer screening by low-dose CT is being widely and rapidly implemented in North America, Europe, Asia, and Australia, there is a critical need for strategies to better define the target population. This is essential to reduce lung cancer mortality while optimizing the balance of benefits and harms associated with screening. The results from this discovery study have been used to develop a fit-for-purpose biomarker assay for lung cancer risk assessment, which is currently being validated in subsequent studies funded by the United States National Cancer Institute (LEAP and INTEGRAL-AT).

Contribution to the MTS implementation
This publication directly addresses Pillars II and III of the MTS 2021–2025, focusing on understanding the causes of cancer and prevention strategies (refer to "Implementing the MTS 2021–2025", IARC MTS 2021–2025, p. 21).

In addition, it aligns with Emerging Priority #2: "Evolving global issues for cancer prevention research", which emphasizes implementation research in the follow-on studies mentioned (Ibid., p. 22).

Publication #6:

Geographic and age-related variations in mutational processes in colorectal cancer
Authors: Díaz-Gay M, dos Santos W, (..), Perdomo S, Stratton MR, Brennan P, Alexandrov LB
References: Nature, Under review

Summary
This study represents the third major publication from the Mutographs project, focusing on the sequencing of 981 colorectal cancer genomes from 11 countries. The analysis revealed multiple signatures, most of which have unknown etiologies, with varying prevalence in Argentina, Brazil, Colombia, the Russian Federation, and Thailand. This suggests geographically diverse levels of mutagenic exposure. Notably, signatures SBS88 and ID18, caused by the bacteria-produced mutagen colibactin, displayed higher mutation loads in countries with higher colorectal cancer incidence rates. SBS88 and ID18 were also enriched in early-onset colorectal cancers; they were 3.3 times as common in individuals diagnosed before age 40 years as in those older than 70 years and were established early in colorectal cancer development.

Scientific, public health, and societal impacts
The rising incidence of early-onset colorectal cancer (diagnosed before age 50 years) is becoming a significant public health issue in many countries. Although there are various hypotheses about the underlying causes, direct evidence has been limited. This study suggests that a key factor behind the increasing incidence may relate to the development of the infant microbiome. Changes in the composition of the infant microbiome over the past 70–80 years could be driving the rise in early-onset colorectal cancer, indicating potential avenues for prevention strategies.

Contribution to the MTS implementation
This publication contributes to Pillars II and III of the MTS 2021–2025 by enhancing understanding of cancer causes, identifying risk factors in transition, and informing prevention strategies (refer to "Implementing the MTS 2021–2025", IARC MTS 2021–2025, p. 21).

➔ **Pillar 3 – From understanding to prevention**

Publication #1:

Cancer Mortality in chrysotile miners and millers, Russian Federation: main results (Asbest Chrysotile Cohort Study)
Authors: Schüz J, Kovalevskiy E, Olsson A, Moissonnier M, Ostroumova E, Ferro G, Feletto E, Schonfeld SJ, Byrnes G, Tskhomariia I, Straif K, Morozova T, Kromhout H, Bukhtiyarov I
References: JNCI; Volume: 116, Issue: 6, Pages: 866–875, June 2024

Summary
This study investigates the relationship between exposure to chrysotile asbestos and cancer mortality among miners and millers in the Russian Federation. The findings reveal an exposure–response between cumulative dust and lung cancer mortality in men. Although no clear association with dust exposure was identified in women, a modest increase in lung cancer risk was observed in the highest category of fibre exposure. Mesothelioma mortality was increased (RR, 7.64; 95% CI, 1.18–49.5, to at least 80 fibres per cm3 years, and RR, 4.56; 95% CI, 0.94–22.1, to at least 150 mg per m3 years, based on 13 deaths). For colorectal and stomach cancer, associations were inconsistent, and no associations were found for laryngeal or ovarian cancer.

Scientific, public health, and societal impacts
Chrysotile continues to be mined and used in many countries globally, presenting clear cancer risks associated with this non-amphibole fibre. These findings have policy implications for the continued mining and use of chrysotile, as well as addressing exposures to chrysotile-containing materials in countries that have already banned its use.

Contribution to the MTS implementation
This research aligns with Pillar II of the MTS 2021–2025: "Understanding the causes of cancer" (refer to "Implementing the MTS 2021–2025", IARC MTS 2021–2025, p. 25), for primary prevention through etiological research.

In addition, it emphasizes the importance of cancer prevention efforts in LMICs, where exposure to hazardous materials such as chrysotile asbestos remains a critical public health concern.

Publication #2:

Treatment guideline concordance, initiation, and abandonment in patients with non-metastatic breast cancer from the African Breast Cancer-Disparities in Outcomes (ABC-DO) cohort in sub-Saharan Africa: a prospective cohort study
Authors: Foerster M, McCormack V, Anderson BO, Boucheron P, Zietsman A, Cubasch H, Joffe M, Anele A, Offiah S, Galukande M, Parham G, Pinder LF, Ginsburg O, Schüz J, Dos-Santos-Silva I, Kantelhardt EJ
References: Lancet Oncology; May 9, 2022

Summary
In this study, 68% of participants with non-metastatic breast cancer underwent surgery. Among women with localized tumours, 36% initiated surgery and systemic therapy (i.e. multimodality treatment) with radiotherapy, compared with 23% of those with locally advanced tumours. Multimodality treatment without radiotherapy was initiated in 386 (38%) women with localized tumours versus 167 (24%) with locally advanced tumours.

Scientific, public health, and societal impacts
This research highlights significant treatment disparities across country-specific groups, revealing low treatment completion rates in all settings. This underscores the need for targeted interventions to improve access to and completion of breast cancer treatment.

Contribution to the MTS implementation
This publication contributes to understanding the drivers of low survival rates for common curable cancers and informs the WHO Global Breast Cancer Initiative. It emphasizes the necessity of focusing on treatment access and completion, rather than solely on achieving downward stage shifts, to effectively address low survival rates in breast cancer patients. This perspective aligns with IARC's goals related to improving cancer outcomes, particularly in LMICs, and addressing health inequalities in vulnerable populations (Emerging Priorities #1 and #3 of the MTS; refer to "Implementing the MTS 2021–2025", IARC MTS 2021–2025, pp. 25–26).

Publication #3:

A portable thermal ablation device for cervical cancer prevention in a screen-and-treat setting: a randomized, noninferiority trial
Authors: Basu P, Mwanahamuntu M, Pinder LF, Muwonge R, Lucas E, Nyambe N, Chisele S, Shibemba AL, Sauvaget C, Sankaranarayanan R, Prendiville W, Parham GP
References: Nature Medicine; Epub ahead of print on 25 June 2024

Summary
This randomized controlled trial aims to demonstrate the noninferiority efficacy of a battery-driven thermal ablation (TA) device compared to cryotherapy and electrosurgical excision (LLETZ) to treat cervical precancer in Zambia. A total of 3124 women who tested positive on VIA and were eligible for ablative therapy were randomized to one of the treatment arms. After a median follow-up of 12 months, the treatment success rates were 74.0% for the TA group, 71.1% for the cryotherapy group, and 71.4% for the LLETZ group.

Scientific, public health, and societal impacts

The study confirmed that a portable thermal ablation (TA) device was an acceptable, effective, and safe method to treat in a screen-and-treat setting. TA offers several important advantages over cryotherapy, including the elimination of expensive consumables, the ability to operate in settings without electricity, and reduced treatment time. The battery-driven thermal ablator developed and evaluated through an IARC project is already being widely used in several sub-Saharan African countries and many other LMICs. In addition, the research demonstrated that TA was cost-effective compared with cryotherapy. The study revealed a significant public health concern: women living with HIV have a nearly 40% treatment failure rate after precancer treatment. This has been identified as a key research priority.

Contribution to the MTS implementation

This research is well aligned with the IARC MTS priority to generate new scientific evidence regarding the effectiveness of implementing primary and secondary prevention interventions (Pillar III, refer to "Implementing the MTS 2021–2025", IARC MTS 2021–2025, p. 25). The findings have led to significant improvement in practice in LMICs, supported by WHO guidelines, thereby translating research into tangible public health outcomes.

Publication #4:

CanScreen5, a global repository for breast, cervical and colorectal cancer screening programmes

Authors: Zhang L, Mosquera I, Lucas E, Rol ML, Carvalho AL, Basu P; CanScreen5 collaborators
References: Nature Medicine; Volume: 29, Pages:1135-1145; April 27, 2023

Summary

The CanScreen5 project is a global cancer screening data repository designed to report the status and performance of cancer screening programmes using a harmonized set of criteria and indicators. Data collected mainly from the ministry of health in each participating country underwent quality validation and ultimately became publicly available through a web-based portal. As of September 2022, 84 countries reported data for breast (n = 57), cervical (n = 75), or colorectal (n = 51) cancer screening programmes. The findings revealed substantial heterogeneity in programme organization and performance; reported screening coverage ranged from 1.7% in Bangladesh to 85.5% in England for breast cancer, 2.1% in Côte d'Ivoire to 86.3% in Sweden for cervical cancer, and 0.6% in Hungary to 64.5% in the Netherlands for colorectal cancer screening.

Scientific, public health, and societal impacts

The CanScreen5 project is a dynamic and ongoing initiative. The team plans to continue engaging with countries, especially LMICs, to enhance data collection and quality. They are optimistic that screening programmes will take advantage of the accelerated digital transformation in the post-COVID era to reform the data collection process. CanScreen5 aims to support countries in building capacity for systematic data collection, ultimately facilitating quality improvement of services. Since the last report, engagement efforts have successfully brought more than 40 new countries into the project, with updates to European data scheduled to begin soon.

Contribution to the MTS implementation

This research is well aligned with the IARC MTS priority to generate new scientific evidence related to the effectiveness of implementing primary and secondary prevention interventions (Pillar III, refer to "Implementing the MTS 2021–2025", IARC MTS 2021–2025, p. 25). By supporting countries in improving the reach and quality of cancer screening services, CanScreen5 directly contributes to making cancer screening programmes more effective and equitable.

Publication #5:

Genome-wide DNA methylation profiling of oesophageal squamous cell carcinoma from global high incidence regions identifies crucial genes and potential cancer markers
Authors: Talukdar FR, Soares Lima SC, Khoueiry R, Laskar RS, Cuenin C, Sorroche BP, Boisson AC, Abedi-Ardekani B, Carreira C, Menya D, Dzamalala C, Assefa M, Aseffa A, Miranda-Gonçalves V, Jeronimo C, Henrique R, Shakeri R, Malekzadeh R, Gasmelseed N, Ellaithi M, Gangane N, Middleton D, Le Calvez-Kelm F, Ghantous A, Roux ML, Schüz J, McCormack V, Parker MI, Ribeiro Pinto LF, Herceg Z.
References: Cancer Research; Volume:81, Pages:2612-2624; May 15, 2021

Summary
This publication led by EGM, in collaboration with IARC and international partners, identifies new epigenetic changes that are specific to oesophageal cancers in high incidence populations (including LMICs). The study represents the largest genome-wide DNA methylation analysis of its kind, examining aberrant epigenome profiles in ESCC samples from nine countries with high disease incidence across Africa, Asia, and South America. The findings demonstrate that alterations in specific genes can identify tumours with high sensitivity and specificity, suggesting potential use as cancer markers for novel prevention strategies in resource-limited settings.

Scientific, public health, and societal impacts
This research identifies robust, tumour-specific molecular (epigenomic) alterations in oesophageal squamous cell carcinoma (ESCC) tumours across several high-incidence populations. The results generated are currently used to advance our knowledge about the causes and prevention of ESCC in areas where it is most prevalent. The identified alterations hold promise as minimally invasive biomarkers, such as those used with Cytosponge technology, which should be prioritized for future early detection and risk stratification efforts.

The feasibility of oesophageal sponge cytology sampling in African settings (Middleton et al., 2021) and ongoing collaborations in China further indicate the potential for these epigenetic markers to be tested and implemented for early detection in various high-incidence populations within low-resource environments.

Contribution to the MTS implementation
This research aligns closely with the IARC MTS, particularly Pillar II: "Understanding the causes of cancer" (refer to "Implementing the MTS 2021–2025", IARC MTS 2021–2025, p. 25). It fulfils Objective 2.2, which aims to enhance understanding of biological mechanisms of carcinogenesis related to environmental and lifestyle factors, including those contributing to cancer disparities. In addition, it supports Objective 2.5 by exploring potential risk factors in under-researched populations, especially in LMICs.

Furthermore, this study significantly contributes to Pillar III: "Understanding the implementation of cancer prevention interventions," specifically Objective 3.3, which focuses on the development and application of biomarkers for early detection and outcomes through translational studies. By identifying actionable biomarkers for ESCC, this research paves the way for improved cancer prevention and intervention strategies in high-incidence settings (Ibid., p. 25).

Publication #6:

Cutaneous and acral melanoma cross-OMICs reveals prognostic cancer drivers associated with pathobiology and ultraviolet exposure
Authors: Vicente ALSA, Novoloaca A, Cahais V, Awada Z, Cuenin C, Spitz N, Carvalho AL, Evangelista AF, Crovador CS, Reis RMR, Herceg Z, Vazquez V de L, Ghantous A
References: Nature Communications;
Volume : 13, Article number: 4115 ; July 15, 2022

Summary
This study integrates clinical and epigenome (DNA methylome), genome, and transcriptome profiling of cutaneous melanoma samples from multi-ethnic cohorts. It identifies UV-related alterations in immunological pathways, with multi-omics cancer driver that may affect patient survival. Notably, the research reveals important features of melanomas that are not associated with UV exposure. A subset of cutaneous melanomas lacked UV mutational signatures, displaying a distinct molecular landscape and clinical prognosis different from those of UV-exposed melanomas but that resembled those of the pathologically distinct acral melanoma. This biological distinction is supported by multi-omics markers of UV exposure critical to immune function. By including patients with varying skin colours, the study enhances the understanding of melanoma origins that may not be triggered by UV exposure, revealing translationally impactful mechanisms in melanoma genesis. The findings promote improvements in conventional protocols for diagnosing, treating, and preventing melanomas.

Scientific, public health, and societal impacts
This study capitalized on archived clinical samples and advanced technologies to construct molecular maps that elucidate genes affecting tumour phenotypes and patient outcome, providing insights into the origins of melanoma development. The inclusion of patients with diverse skin colours broadens the spectrum of melanoma forms studied, facilitating a better understanding of non-UV-triggered melanoma origins. Importantly, the study highlights the similarities between cutaneous melanomas without UV exposure and acral melanoma, showcasing significant gene–environment interactions across different ethnic backgrounds. There is a growing interest in personalized approaches in the treatment and prevention of cancer (including melanoma), considering differences in the molecular architecture of individual tumours and potentially preventable causes. The work also generated interdisciplinary evidence for improving conventional protocols of diagnosing and treating as well as preventing melanomas. The research also addresses the urgent need for ethnic diversification in cancer research, specifically by incorporating under-represented ethnicities from LMICs.

Contribution to the MTS implementation
This research directly contributes to the MTS 2021–2025, specifically Pillar II: "Understanding the causes of cancer". It notably addresses Objective 2.2: "Enhance understanding of and elucidate biological mechanisms of carcinogenesis relevant to environmental/lifestyle factors, including those that accompany key cancer transitions, and those related to cancer disparities, through the conduct of laboratory studies", and Objective 2.5: "Enhance understanding of potential risk factors, including those that accompany key cancer transitions, and those related to cancer disparities, in under-researched populations and/or in LMIC and their interplay with the observed cancer patterns".

➔ **Pillar 4 – Knowledge mobilization**

Publication #1:

Carcinogenicity of occupational exposure as a firefighter
Authors: Demers PA, DeMarini DM, Fent KW, Glass DC, Hansen J, Adetona O, Andersen MH, Freeman LEB, Caban-Martinez AJ, Daniels RD, Driscoll TR, Goodrich JM, Graber JM, Kirkham TL, Kjaerheim K, Kriebel D, Long AS, Main LC, Oliveira M, Peters S, Teras LR, Watkins ER, Burgess JL, Stec AA, White PA, DeBono NL, Benbrahim-Tallaa L, de Conti A, El Ghissassi F, Grosse Y, Stayner LT, Suonio E, Viegas S, Wedekind R, Boucheron P, Hosseini B, Kim J, Zahed H, Mattock H, Madia F, Schubauer-Berigan MK.
References: The Lancet Oncology; Volume: 23, Issues: 8, Pages: 985-6, June 30, 2022

Summary
This publication evaluates the carcinogenic hazard evaluation of firefighting exposure. Firefighting was classified as carcinogenic to humans (Group 1), with sufficient evidence for mesothelioma and bladder cancer and limited evidence for cancers of the colon, prostate, testis, non-Hodgkin

lymphoma, and skin melanoma in humans. In addition, the article presents strong mechanistic evidence in humans for five key characteristics of carcinogens: genotoxicity, epigenetic alterations, oxidative stress, chronic inflammation, and modulation of receptor-mediated effects.

Scientific, public health, and societal impacts

This article has been cited more than 150 times in the scientific literature and policy documents globally. The cancer hazard classification in Group 1 has led to hundreds of actions taken by researchers, fire services, and governments around the world to reduce exposures to carcinogens among paid and unpaid firefighters, and to compensate firefighters for occupationally induced cancers. New research is being conducted to better document exposures and methods to reduce them.

Contribution to the MTS implementation

This publication documents the work of IARC Monographs Working Group 132 to identify carcinogenic hazards to humans. The large number of citations is attributed to the high degree of interest and public health relevance to the more than 15 million firefighters worldwide. This research aligns with IARC's mission to enhance understanding of cancer risks (Pillar II) and inform prevention strategies (Pillar III, refer to "Implementing the MTS 2021–2025", IARC MTS 2021–2025, p. 25).

Publication #2:

Carcinogenicity of perfluorooctanoic acid and perfluorooctanesulfonic acid
Authors: Zahm S, Bonde JP, Chiu WA, Hoppin J, Kanno J, Abdallah M, Blystone CR, Calkins MM, Dong GH, Dorman DC, Fry R, Guo H, Haug LS, Hofmann JN, Iwasaki M, Machala M, Mancini FR, Maria-Engler SS, Møller P, Ng JC, Pallardy M, Post GB, Salihovic S, Schlezinger J, Soshilov A, Steenland K, Steffensen IL, Tryndyak V, White A, Woskie S, Fletcher T, Ahmadi A, Ahmadi N, Benbrahim-Tallaa L, Bijoux W, Chittiboyina S, de Conti A, Facchin C, Madia F, Mattock H, Merdas M, Pasqual E, Suonio E, Viegas S, Zupunski L, Wedekind R, Schubauer-Berigan MK
References: The Lancet Oncology; Volume: 25, Issues: 1, Pages: 16-17, November 30, 2023

Summary

This publication evaluates the carcinogenic hazards of perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS). PFOA was classified as carcinogenic to humans (Group 1), based on sufficient evidence of cancer in experimental animals and strong mechanistic evidence, including epigenetic alterations and immunosuppression in exposed humans. There was also limited evidence for cancers of the testis and kidney (renal cell carcinoma) in humans. In contrast, PFOS was classified in Group 2B based on strong mechanistic evidence, including in exposed humans.

Scientific, public health, and societal impacts

PFOA and PFOS occur ubiquitously in the environment, with high levels at pollution sources such as industrial sites and in firefighter training areas, waste deposits, and contaminated wastewater. PFOA and PFOS may also be present in contaminated food, especially fish, seafood, and eggs. Occupationally exposed populations have some of the highest levels of exposure, mainly via inhalation. The general population in communities that are not near pollution sources is mainly exposed to PFOA and PFOS via diet and drinking-water. This publication has been cited more than 60 times in less than 1 year, indicating great interest by the research community.

Contribution to the MTS implementation

This publication documents the work of IARC Monographs Working Group 135 to identify carcinogenic hazards to humans. The large number of citations is attributed to the high degree of interest and public health relevance to the hundreds of millions of people worldwide exposed to these two legacy PFAS compounds, PFOA and PFOS, through the workplace, food, drinking-water, and elsewhere in the environment. This research aligns with IARC's mission to enhance understanding of cancer risks (Pillar II) and inform prevention strategies (Pillar III, refer to "Implementing the MTS 2021–2025", IARC MTS 2021–2025, p. 25).

Publication #3:

WHO Classification of Tumours. Paediatric tumours
Authors: WHO Classification of Tumours Editorial Board
References: *WHO Classification of Tumours Editorial Board. Paediatric tumours; WHO classification of tumours series, 5th edition; Volume: 7*, 2023

Summary
This new volume in the 5th edition was implemented to support the WHO Global Initiative for Childhood Cancer by supporting the correct diagnosis, thereby promoting correct patient management, prognosis, and further research.

Scientific, public health, and societal impacts
This volume is continuing to have a tremendous impact on the correct diagnosis, management, and prognosis of children with cancer while supporting further research in areas ranging from etiology to early diagnosis and prevention of childhood cancers, thereby contributing to better health outcomes for affected children and their families.

Contribution to the MTS implementation
The 5th edition of the WHO Classification of Tumours ("Blue Books") is an essential contributor to Pillar IV: "Synthesizing and mobilizing knowledge and strengthening global capacities in cancer science" (refer to "Implementing the MTS 2021–2025", IARC MTS 2021–2025, p. 25), providing the authoritative recommendations used worldwide in tumour classification.

Publication #4:

WHO Classification of Tumours. Haematolymphoid tumours
Authors: WHO Classification of Tumours Editorial Board
References: WHO Classification of Tumours Editorial Board. Haematolymphoid tumours; WHO classification of tumours series, 5th edition; Volume: 10; 2024

Summary
This volume in the 5th edition is highly regarded not only by pathologists and haematologists but also by clinicians and oncologists. This publication promotes correct management of patients affected by haematological malignancies, affects their prognosis, and initiates further research, especially molecular-based research in the current era.

Scientific, public health, and societal impacts
This volume significantly affects the correct diagnosis, management, and prognosis of patients with haematological malignancies while supporting further research in addition to molecular-based research, in areas ranging from etiology to early diagnosis and prevention of haematological malignancies.

Contribution to the MTS implementation
The 5th edition of the WHO Classification of Tumours ("Blue Books") is an essential contributor to Pillar IV of the IARC MTS: "Synthesizing and mobilizing knowledge and strengthening global capacities in cancer science" (refer to "Implementing the MTS 2021–2025", IARC MTS 2021–2025, p. 25), providing the authoritative recommendations used worldwide in tumour classification.

Publication #5:

The IARC Perspective on Cervical Cancer Screening
Authors: Bouvard V, Wentzensen N, Mackie A, Berkhof J, Brotherton J, Giorgi Rossi P, Kupets R, Smith R, Arrossi S, Bendahhou K, Canfell K, Chirenje ZM, Chung MH, del Pino M, de Sanjosé S, Elfström M, Franco EL, Hamashima C, Hamers FF, Herrington CS, Murillo R, Sangrajrang S, Sankaranarayanan R, Saraiya M, Schiffman M, Zhao F, Arbyn M, Prendiville W, Indave Ruiz BI, Mosquera Metcalfe I, Lauby Secretan B.

References: New England Journal of Medicine (NEJM); Volume: 385, Issues: 20, Pages: 1908-1918; November 10, 2021

Summary

This publication presents the findings of a Working Group of international experts who evaluated the effectiveness of all currently used cervical screening methods in reducing cancer incidence and mortality. The methods assessed included cytology, liquid-based cytology, HPV testing, visual inspection with acetic acid (VIA), and Romanowsky–Giemsa staining. In addition, the Working Group reviewed and formulated a consensus statement on the comparative effectiveness of HPV tests compared with cytology and compared with co-testing.

Scientific, public health, and societal impacts and contribution to the MTS implementation

Published in a highly recognized scientific journal with an impact factor of 96.2, the findings serve as a foundational basis for the updated "WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention". These guidelines have a significant impact on public health policies aimed at improving cervical cancer prevention globally.

Report: IARC collaboration mapping 2021-2024

Objectives

Effective collaboration is essential to IARC's mission, allowing the agency to build and strengthen relationships with key stakeholders to enhance its global impact. The IARC collaboration mapping aims to provide a comprehensive overview of the organization's ecosystem, offering detailed insights into key stakeholders, the nature of their interactions, and their level of influence. This evidence-based approach enables IARC to strategically prioritize its efforts and resources, focusing on fostering and cultivating the most impactful partnerships for its mission.

This exercise will also serve as a foundation for identifying key stakeholders to be interviewed as part of a collective effort in developing the IARC Medium-Term Strategy (MTS) for 2026–2030.

Methodology

Data extraction

The first step in the collaboration mapping process involved extracting comprehensive data on all IARC collaborations for the 2021–2024 period. Various sources were used to compile a complete list of entities that have collaborated with IARC, both as funders and as research partners:

- **Web of Science (WoS):** IARC publications from 2021–2024 were extracted using this bibliometric tool. The dataset included 1218 research papers in which IARC participated, of which 309 were led by IARC. In addition to identifying research collaborators, this dataset also included funding entities, extracted through funding acknowledgments from the papers where IARC was the lead. This process yielded 470 unique funders from a total of 2470 data points.
- **Collaborative Research Agreements (CRAs):** Data from IARC's SAP system provided information on 199 CRAs signed during the MTS period. The funding amounts associated with these agreements were also extracted to categorize the level of collaboration.
- **Expert lists:** The *WHO Classification of Tumours* ("WHO Blue Books"), IARC Handbooks, and IARC Monographs experts who contributed to IARC's projects during the period were also included. A total of 2949 collaborations with experts from 517 different organizations were recorded.
- **Project Portal and FENSA data:** Internal project data from IARC's Project Portal, listing projects with external budgets, were integrated and cross-referenced with corresponding publications in WoS to avoid duplicate records. The FENSA risk register, which tracks IARC's collaboration with private sector entities, was used to categorize private sector funders for these projects.

Data standardization

Collaborations were classified as either direct or supporting collaborations:

- **Direct collaborations:** IARC-led research papers, CRAs, funders providing direct financial support, and experts mandated by IARC were all considered direct collaborations.
- **Supporting collaborations:** These included instances where IARC participated as a collaborator but did not lead the research effort.

Organizations were classified into 18 specific legal status types and then grouped into five broader categories for simplified analysis:

- **Governmental and Intergovernmental organizations**
- **Private not-for-profit**
- **Private for-profit**
- **Academic institutions and research facilities**
- **Hospitals**

Institutions that are part of larger legal entities but manage independent budget and research programmes (e.g. Harvard University and its various schools) were treated as separate entities, recognizing their autonomy in choosing collaborators. Conversely, regional or municipal governments and their subdivisions were aggregated into single entities to minimize discrepancies arising from differences in regional governance structures.

Collaborators were further categorized based on their level of interaction with IARC during the 2021–2024 period. A five-tier scale was developed to quantify the frequency and depth of interaction:

- **Level 1:** Supporting collaborations.
- **Level 2:** 1–9 direct collaborations or less than €50 000 in funding over the period (either received by IARC or provided to collaborators through CRAs).
- **Level 3:** 10–20 direct collaborations or between €50 000 and €100 000 in funding.
- **Level 4:** 21–49 direct collaborations or between €100 000 and €500 000 in funding.
- **Level 5:** More than 50 direct collaborations or more than €500 000 in funding.

Results part one: IARC ecosystem

Overview

➔ IARC's collaborations in 2021–2024 are extensive, spanning a wide range of stakeholders, particularly research institutions and public sector entities. The Agency's efforts are globally distributed, with a strong emphasis on partnerships in LMICs, aligning with its mission to reduce the global cancer burden.

Outputs:

- During the 2021–2024 period, IARC had **38 895 collaboration points** across all categories, involving **2263 unique organizations**. A substantial proportion of these collaborations came from co-publications (28 595 collaborations), which underscores IARC's focus on producing research outputs with a wide range of partners. When only direct collaborations were considered, there were **10 300 collaboration points** involving **1405 unique organizations**.

Types of collaborators:

- Across all collaboration types, **research institutions** remain the dominant collaborators, making up **62%** of the total organizations. For co-publications, 71% involved research institutions.
- The **public sector** dominates IARC's collaborations, accounting for **81%** of total partnerships. This is even more pronounced in co-publications (85%) and research funders (78%), with **50% of IARC's research funders classified as governmental or intergovernmental organizations**. This underscores the strong public sector engagement in IARC's work.
- **Private not-for-profit** organizations represent **4%** of IARC's total collaborators, with slightly higher engagement (11%) in CRAs. This suggests a **specific role for these organizations in formal agreements**, but overall, they make up a smaller proportion of IARC's collaborations.
- **Private for-profit entities** represent the smallest segment of IARC's collaborators, making up only 2% of total collaborations (with less than 1% in direct collaborations and no funding

sourced from this sector). This low representation is expected, given IARC's limited and carefully regulated engagement with the private sector.

- **Hospitals** are significant collaborators in co-publications (19%) and CRAs (23%), underlining the clinical impacts of IARC's cancer research. Hospitals are more engaged in **expert contributions (33%),** showing their importance in advisory roles.

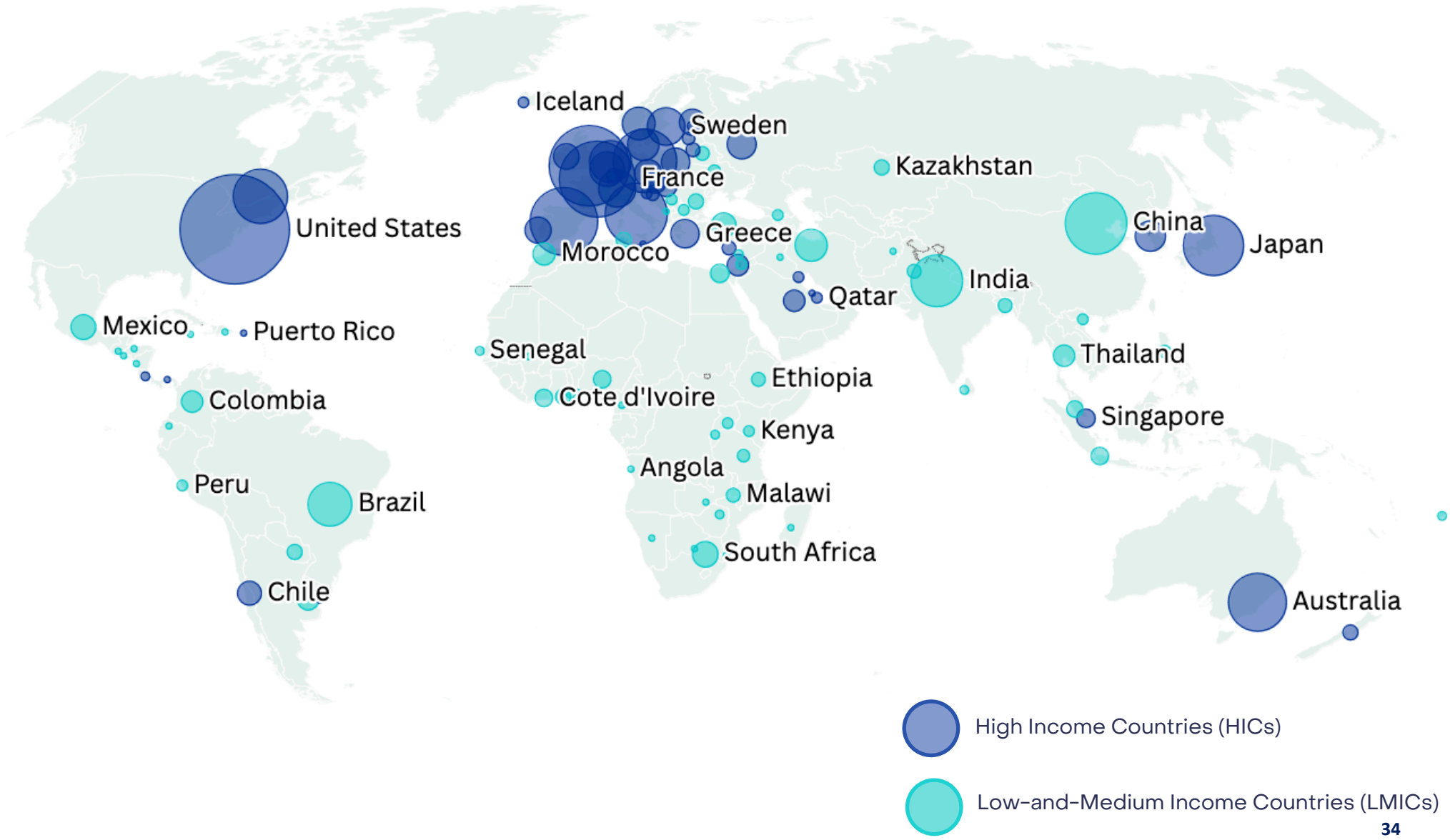
Geographical range:

- IARC collaborated with partners from **123 countries in total and 91 for direct collaborations** (see the map below).
- IARC's collaboration with **LMICs** is a significant feature of its partnerships. Across all collaboration types, **24% of collaborations** involved LMICs, and **50% of CRAs** specifically involved LMIC partners. The higher LMIC involvement in CRAs indicates IARC's strategic focus on engaging with resource-limited settings for structured, long-term agreements.
- **Experts** involved in the WHO Blue Books, *IARC Monographs*, and *IARC Handbooks* mainly represented the **public sector (75%), with 28% from LMICs**, indicating that although the expert groups are predominantly from high-income settings, reflecting the concentration of advanced research in these regions, there is still meaningful inclusion from lower-resource environments.

Table 1. Breakdown of IARC collaborations in 2021–2024 across different categories of interaction.

Collaboration type	Total collaborations	Unique collaborating organizations	% Governmental and IGO	% Not-for-profit	% Private for-profit	% Research organizations	% Hospitals	% Public sector	# of countries	% LMICs
Co-publications (all)	28 595	1 668	7%	1%	2%	71%	19%	85%	117	26%
Co-publications (IARC Lead)	4,683	798	9%	2%	0%	68%	21%	86%	78	19%
Expert contributions	2 945	517	6%	1%	0%	60%	33%	75%	39	15%
Research funders	2470	360	50%	19%	0%	25%	6%	78%	51	14%
CRAs	199	109	11%	11%	1%	55%	22%	66%	45	50%
Total (all)	38 895	2263	12%	4%	2%	62%	20%	81%	123	24%
Total (direct collaborations)	10 300	1405	18%	6%	1%	54%	21%	80%	91	20%

Map of IARC direct collaborations in 2021-2024:



Map of IARC direct collaborations in 2021–2024 (Europe):

Level of interaction

The second part of the analysis focuses on identifying IARC's key collaborators by assigning each entity a corresponding level of interaction with IARC, based on the five-tier scale outlined in the methodology. This approach enables a more qualitative understanding of the IARC ecosystem, offering insights into the depth and frequency of collaboration with each partner.

➔ Distribution of collaborations by interaction level

- **Level 1 (supporting collaborations)**: **38%** of organizations fall into this category. These are partners where IARC's involvement was more peripheral, often as a participant in multi-party collaborations. This high percentage is expected because IARC is often involved in large international research networks where multiple organizations contribute to a single project.
- **Level 2 (1-9 direct collaborations or less than €50,000 in funding)**: **51%** of organizations are in this category, representing IARC's broad connections. These are typically lower-intensity collaborations but nonetheless important for expanding IARC's research and collaboration network.
- **Level 3 (10-20 direct collaborations or less than €100,000 in funding)**: **4%** of organizations, where the collaboration is notable in both frequency and funding.
- **Level 4 (21-49 direct collaborations or €100,000-€500,000 in funding)**: **4%** of organizations reached this level, representing key collaborators for IARC, in terms of both funding amounts and the frequency of engagements.
- **Level 5 (more than 50 direct collaborations or more than €500,000 in funding)**: **3%** of organizations (34 organizations and 29 Participating States) represent IARC's closest and most important partners. These entities, along with Level 4 collaborators, are critical to IARC's research, funding, and policy influence, forming the core of its collaborative network.

➔ Key collaborators: Analysis of level 3, 4 and 5 organizations

This analysis focuses on IARC's core collaboration ecosystem, comprising 243 organizations classified under **Level 3**, **Level 4**, and **Level 5** of the five-tier interaction scale. The complete list is included in the annex.

Geographical distribution:

- **HICs** dominate the key collaboration list, particularly from **Western Europe** (France, Germany, UK, Netherlands, Spain) and **North America** (USA, Canada). This reflects IARC's focus on partnerships with well-established institutions that have advanced research capabilities and strong funding mechanisms.
- **LMICs,** although less represented, remain significant contributors to IARC's collaborations, with countries such as **India**, **Mexico**, and **Zimbabwe** playing key roles, particularly through **CRAs** and partnerships with **private not-for-profit entities**.

Types of key collaborators:

- **Intergovernmental/governmental organizations (28%):** In addition to IARC's Participating States, key partners include entities such as the European Commission (EC) and the World Health Organization (WHO). Various ministries of health also support IARC's research through

voluntary contributions or other mechanisms, further reinforcing their role beyond their participation as IARC's Participating States.

- **Not-for-profit (11%):** Organizations such as the Bill & Melinda Gates Foundation, World Cancer Research Fund, and Cancer Research UK play a pivotal role in IARC's collaborations by providing essential financial and operational resources. Although not-for-profit entities account for only 4% of IARC's total collaborations, they constitute a larger proportion of its key collaborators, underscoring the significant funding opportunities they offer.
- **Research institutions (48%)** and **hospitals (12%)** make up the largest groups of IARC's collaborators, with key partnerships (Levels 4–5) including prominent institutions such as Umeå University (Sweden), University of Oxford (UK), and Harvard University (USA). Among hospital collaborators, significant partnerships include Massachusetts General Hospital (USA), Mayo Clinic (USA), and Memorial Sloan Kettering Cancer Center (USA).
- The **public sector** represents **74%** of IARC's key collaborators, a slightly lower proportion than in IARC's total collaborations (81%), highlighting the growing importance of the **private sector** within IARC's core network and as funding partners.

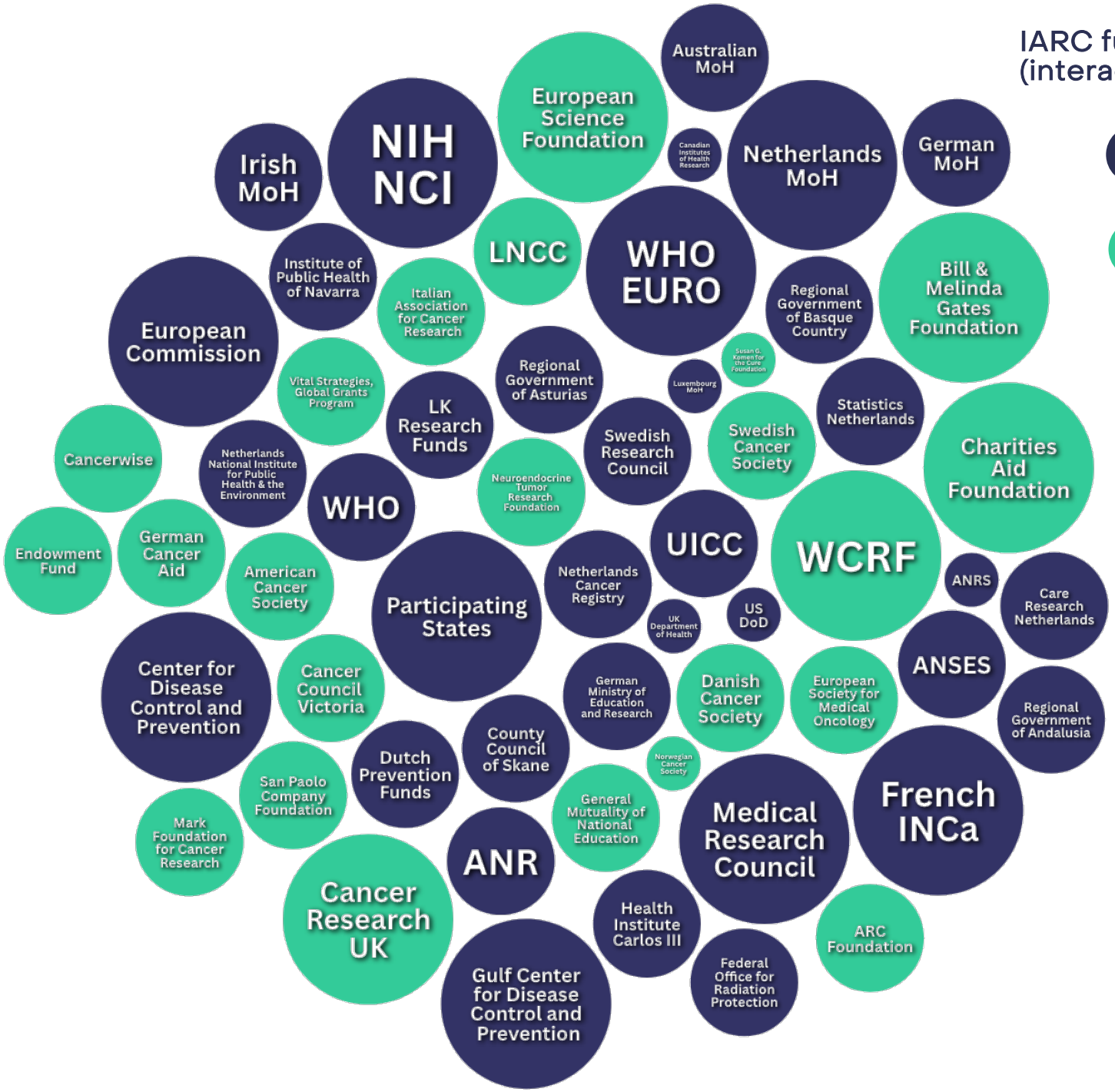
Key collaborators by country:

- **USA:** With 52 collaborating institutions, the USA has the highest representation, with 65% are research institutions and 7% are governmental organizations, including the NIH National Cancer Institute as a key collaborator.
- **France:** With 22 collaborating institutions, France has a higher proportion of governmental organizations (19%) and 43% are research institutions. Among Level 4–5 collaborators, France leads with key partners such as INSERM, UNICANCER, and Université Paris-Saclay, underscoring its central role in IARC's core network.
- **Spain:** Spain is close behind, with 21 collaborating organizations, of which 35% are governmental entities, reflecting Spain's strong engagement with IARC's initiatives.
- **UK:** The UK is well represented, with key partners including Cancer Research UK, Imperial College London, and the University of Oxford.
- **India and Mexico:** These LMICs are the most prominent among IARC's key collaborators, while Zimbabwe also plays a notable role, with institutions such as the University of Zimbabwe and the Harare Health and Research Consortium.

Visual representation of IARC's key collaborators:

The bubble charts below illustrate IARC's ecosystem, segmented into two main groups: IARC funders and the IARC scientific community. Notably, within the scientific community, several organizations have played a dual role by contributing funding to IARC during the MTS period—through either direct funding or competitive grants—while also serving as scientific collaborators (e.g. INSERM, Imperial College London). These dual-role organizations act as both financial supporters and research partners. A detailed list at the end of this exercise specifies which organizations fulfill this dual function.

IARC funders (interaction levels 3, 4, and 5)



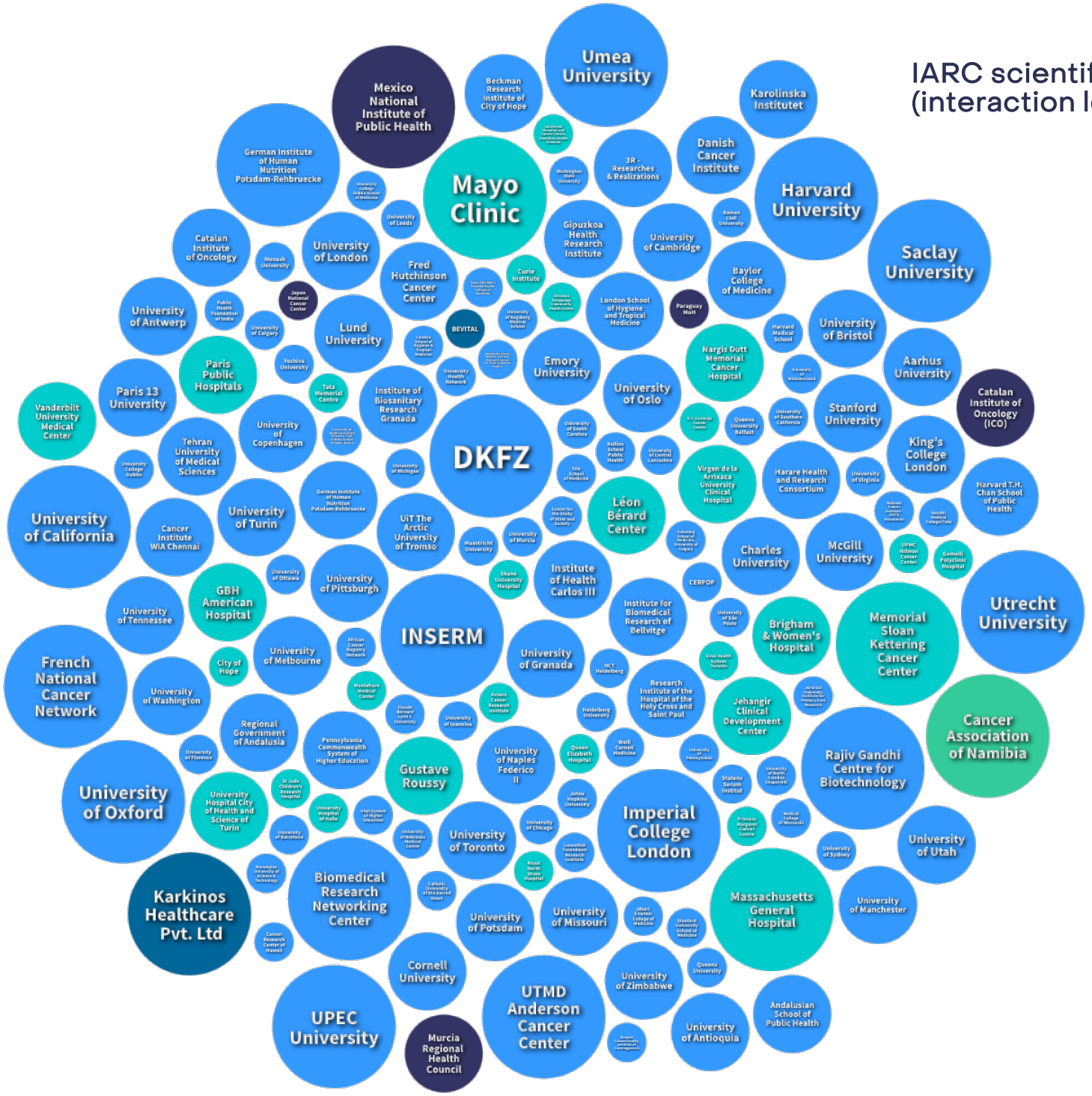
Governmental and IGOs

Not-for-profit organizations

Top countries from IARC funders (governmental entities) include:

1. Netherlands
2. France
3. Spain
4. Germany
5. UK
6. USA
7. Sweden
8. Canada
9. Italy
10. Australia
11. Saudi Arabia
12. Ireland

IARC scientific community (interaction levels 3, 4, and 5)



- Research organizations
- Hospitals
- Governmental and IGOs (non-resource-based collaboration)
- Private not-for-profit (non-resource-based collaboration)
- Private for-profit (non-resource-based collaboration)

Top countries from the IARC scientific community include:

1. USA
2. Spain
3. UK
4. France
5. Canada
6. Italy
7. Germany
8. India
9. Australia
10. Denmark
11. Sweden
12. Norway

Results part two: IARC's unique value in orchestrating international collaboration

The second part of this study takes a more analytical approach, examining the data presented earlier to address a key question:

➔ **While IARC collaborates extensively with organizations worldwide, does it bring unique value in leading international collaboration?**

In today's hyperconnected research landscape, having a large network of collaborators is increasingly common and does not inherently signify a unique leadership role. To determine whether IARC holds a distinct advantage, we must examine the impact of these collaborations, particularly in terms of stimulating international research efforts, and measure this impact relative to other major institutions.

To assess IARC's position within the global cancer research ecosystem, we use three indicators:

1. **Stimulation of research collaboration with IARC's Participating States**
2. **Integration of key cancer research leaders within IARC's network**
3. **Benchmarking IARC amongst other leading cancer research institutions**

1. Stimulating research collaboration with IARC Participating States

We first evaluated IARC's collaborative impact within its Participating States to determine whether these countries derive added value from their investment in IARC through increased collaboration. While a high rate of collaboration with Participating States does not alone prove IARC's leadership in international collaboration – because non-Participating States are also key players in cancer research – it strongly suggests that IARC plays a pivotal role in fostering and stimulating research within its Participating States.

➔ The results demonstrate that a **significant majority of IARC's collaborations are with entities in Participating States**. In 2021–2024, **84% of the organizations** IARC collaborated with were based in its Participating States, even when excluding funding entities and focusing solely on direct research collaborations (83%). In comparison, Participating States are involved in **71%** of supporting collaborations, where IARC is not leading. This indicates that when IARC takes a leading role in research, there is a notable increase in the participation of its Participating States in these collaborations.

➔ In addition, **95% of IARC's key collaborators (Levels 4 and 5)** – those with the most frequent and meaningful interactions – are from Participating States (see Results part one).

Key collaborators outside IARC Participating States:

While most of IARC's key collaborators are from Participating States, some important partnerships exist with institutions in non-Participating States, particularly in LMICs. These collaborations offer strong potential for future membership:

- **Mexico** and **Namibia**: These two non-Participating States have established crucial collaborations with IARC, specifically through the National Institute of Public Health of Mexico and the Cancer Association of Namibia.
- **Colombia** and **Zimbabwe**: In Level 4 collaborations, Colombia and Zimbabwe have also emerged as important partners, with institutions such as the University of Antioquia (Colombia) and the University of Zimbabwe and Harare Health and Research Consortium playing vital roles in regional cancer research initiatives.
- In addition, countries such as **South Africa, Argentina**, and **Greece** maintain a significant number of collaborations with IARC, although these partnerships are more frequent at lower levels (below Levels 4 and 5), demonstrating strong engagement across numerous projects.

2. Assessing IARC's integration with global cancer research leaders

To further assess IARC's unique value in leading international collaboration, we compared its collaborative network with key actors from the global cancer research ecosystem. The goal was to determine whether IARC's research network includes the major players in cancer research, which would suggest that IARC covers a substantial proportion of collaborative cancer research efforts.

We identified the major actors in the cancer research ecosystem using three criteria:

- **Research outputs**: Leading institutions and countries that produce the most cancer research publications.
- **Research funding**: Major public and private cancer research funders.
- **Cancer control efforts** using the list of members of the Union for International Cancer Control (UICC), which includes the world's major cancer leagues, research institutes, treatment centres, hospitals, ministries of health, public health agencies, and patient support groups.

Research collaboration with leading organizations and countries:

We analysed the top 200 organizations and the top 100 countries producing the most cancer research papers in 2021–2024, using research outputs in the Web of Science oncology category to identify the most active institutions and countries.

- During this period, IARC collaborated with **99% of the top 200 organizations**. The only organizations without recorded collaborations were Harbin Medical University (China) and the Japanese Foundation for Cancer Research.
- In terms of countries leading cancer research, IARC directly collaborated with **96% of the top 100 countries**. The exceptions were Algeria, Oman, Uzbekistan, and Sudan.

Collaboration with major research funders:

To assess IARC's engagement with key funders, we analysed the top 200 most acknowledged cancer research funders, based on funding acknowledgments in the Web of Science oncology category. This list was further supplemented with data from the Health Research Funder Database (https://www.healthresearchfunders.org), compiled by WHO researchers, which ranks organizations for their research and development spending.

- Out of 256 identified funding organizations, IARC has collaborated with or received funding from **41%**. This relatively low coverage can be explained by several factors:
  - Many of these organizations are private, for-profit entities (e.g. Novartis, Bristol Myers Squibb), with which IARC is restricted from collaborating.
  - A number of funders primarily support local research efforts through grants to universities or regional public funding schemes.
- Nevertheless, there remains potential to explore partnerships with funders that align with IARC's mission, such as the **Movember Foundation**, the **French Foundation for Medical Research (FRM)**, or the **Avon Foundation for Women**.

Engagement with UICC members:

We also compared IARC's network with the UICC membership list.

- IARC collaborates with **36% of UICC members**. Although this figure is lower, it is important to note that a significant proportion of UICC members are small regional organizations focused on treatment or advocacy, areas outside of IARC's core mission. In addition, IARC collaborates closely with UICC itself, indirectly impacting many of these members.

➔ Nevertheless, this presents opportunities for expanding partnerships and securing funding, especially with UICC members in **LMICs**, where IARC's expertise in research could complement local efforts.

3. Leading the global collaborating efforts

To evaluate IARC's capacity to lead global cancer research collaboration, we conducted a benchmarking analysis comparing IARC's performance with that of major institutions known for producing high volumes of cancer research.

We began by selecting a sample of 12 institutions from the top 50 global producers of cancer research publications (identified in the previous section), ensuring a balanced representation across different regions. The selected institutions were:

- Harvard Medical School (USA)
- UT MD Anderson Cancer Center (USA)
- University of Toronto (Canada)
- Institut National de la Santé et de la Recherche Médicale (INSERM) (France)
- German Cancer Research Center (DKFZ) (Germany)
- Chinese Academy of Medical Sciences/Peking Union Medical College (China)
- Fudan University (China)
- Imperial College London (UK)
- Karolinska Institutet (Sweden)
- Fondazione IRCCS Istituto Nazionale dei Tumori (Italy)
- Erasmus MC (Netherlands)
- University of Sydney (Australia)

For this benchmarking, we focused exclusively on research collaborations reflected in co-authored publications and excluded collaborations related to funding or expert participation. This approach ensures consistency, because we lack comparable data on funding and expert collaborations for the other institutions in the analysis. This analysis focuses exclusively on **direct collaborations (Levels 2–5)** to evaluate IARC's role in driving impactful global partnerships.

The results are displayed in Table 2 below:

➔ This benchmarking analysis shows that despite its smaller size and expected smaller publication output compared with major institutions such as Harvard, MD Anderson, and Fudan University, **IARC outperforms many of these organizations** in terms of global collaboration and its ability to connect with diverse research institutions across the world.

➔ IARC shows a strong collaboration effort, with **4683 collaborations**, which is significant given its size. Institutions such as Harvard and MD Anderson have significantly higher paper outputs, making their collaboration-to-paper ratio lower. When collaborations are compared relative to size, **IARC's collaboration network is far more extensive** than expected, indicating that IARC is leveraging its partnerships effectively to punch above its weight in terms of research collaborations.

➔ IARC leads the benchmark in terms of collaborators per paper, with **15 collaborators per paper**, **the highest among all institutions**. In comparison, larger institutions such as MD Anderson (3.8), Harvard (8.2), and Fudan University (1.3) have far fewer collaborators per paper. DKFZ (11.4) and INSERM (14.8) come closest to IARC but still fall short.

➔ IARC works with **828 unique organizations**, which is highly competitive even when compared with institutions with much larger outputs, such as Harvard (1246) and MD Anderson (1143). This shows that IARC's collaboration network spans across a large number of institutions. Imperial College and DKFZ, with 476 and 660 unique organizations, respectively, are significantly behind IARC in terms of the breadth of collaboration.

➔ IARC again leads in terms of unique organizations per paper, with an average of **2.7 unique organizations per paper**, far ahead of most other institutions. By comparison, Harvard (0.7), MD Anderson (0.5), and Fudan University (0.2) work with fewer unique partners per paper,

indicating that IARC's research outputs are more collaborative and internationally diverse. Imperial College comes close with 2.3 unique organizations per paper. This indicator is particularly telling of IARC's leadership in fostering international collaboration; when we consider all publications involving IARC (including those where it is not the lead), this number drops to 1.4. The fact that IARC doubles its number of unique collaborators when leading a publication underscores its strong role in driving international research partnerships.

- IARC collaborates with institutions from **78 countries**, the highest figures in the table, surpassing Harvard (71 countries) and the University of Toronto (74 countries). Institutions such as Fudan University (28 countries) and CAMS (28 countries) have a more regional focus, engaging with fewer countries overall.
- In addition, IARC shows a stronger commitment to **LMICs** than many other institutions, with **18%** of its collaborations involving LMICs, placing it ahead of several other institutions. CAMS and Fudan University show higher percentages, but this is largely due to their regional collaborations within China. When collaborations with China are excluded, IARC's 18% LMIC engagement outperforms their adjusted LMIC rates (CAMS drops to 6%, and Fudan University drops to 3% without China). Karolinska Institutet (17%), Harvard (16%), and MD Anderson (15%) also have strong LMIC engagements, but IARC's focus remains a defining feature of its international collaboration strategy. However, given IARC's mandate as an international agency, the 18% figure may still appear modest, suggesting that there is room for IARC to expand its collaborative efforts with LMICs. This strategy is already being pursued through CRAs, as noted above.

Table 2. Benchmarking IARC amongst leading cancer research institutions (publications in 2021–2024).

Institution	Total publications	Total collaborations	Collaborations per publication	Unique collaborating organizations	Unique organizations per publication	Countries involved	% of Collaborations with LMICs
IARC	**309**	**4683**	**15**	**828**	**2.7**	**78**	**18%**
DKFZ	465	5304	11.4	660	1.4	54	9%
Imperial College	208	2083	10	476	2.3	49	8%
MD Anderson	2239	8461	3.8	1143	0.5	65	15%
IRCCS (Milan)	421	3201	7.6	569	1.4	42	4%
Harvard	1898	15490	8.2	1246	0.7	71	16%
Inserm	379	5607	14.8	533	1.4	47	8%
CAMS	2275	2065	0.9	471	0.2	28	52% (6% without China)
University of Toronto	1567	15286	9.8	1202	0.8	74	11%
Fudan University	2413	3193	1.3	512	0.2	28	41% (3% without China)
Erasmus MC	560	2926	5.2	551	1.0	43	4%
University of Sydney	350	2530	7.2	448	1.3	34	8%
Karolinska Institutet	612	2229	3.6	461	0.8	51	17%

Key insights

A key limitation of this analysis is that it captures only **formalized collaborations**, derived from sources such as co-author affiliations, funding acknowledgments, and signed agreements. However, IARC also engages in extensive **informal collaborations** that are not fully reflected here, such as providing **expertise** to various entities and participating in **steering committees** (e.g. IARC is a member of the International Advisory Board of the National Liver Disease Biobank in India and a member of the Scientific Advisory Board of the Lung Cancer Research Foundation in the USA). In addition, IARC's **Regional Hubs through the Global Initiative for Cancer Registry Development (GICR) initiative**[17] impact several countries not represented in these formalized data. Therefore, IARC's collaborative reach is likely to be broader than what this analysis shows.

Nonetheless, this overview offers valuable insights into IARC's key collaborators and its positioning within the cancer research ecosystem. The analysis highlights IARC's unique strength in connecting with a wide array of organizations and coordinating global cancer research efforts.

Key takeaways include:

- **Collaborative focus on research institutions**: Research institutions are at the heart of IARC's key collaborations, reinforcing its mission to generate and disseminate scientific knowledge on cancer prevention and control. IARC's partnerships with leading actors in the cancer research ecosystem reflect high standards of research excellence.
- **Leadership in international collaboration**: Despite its smaller size compared with institutions such as Harvard and MD Anderson, IARC excels in collaboration diversity and breadth, leading the way in multi-institutional partnerships. It has the highest numbers of collaborators per paper and unique organizations per paper.
- **Global reach and LMICs engagement**: IARC's collaboration network spans 123 countries, with strong ties to LMICs. It excels in fostering long-term, sustainable partnerships, particularly through CRAs, which emphasize its commitment to addressing cancer research needs in resource-limited regions.
- **Strong public sector engagement**: With 81% of its collaborators being publicly funded entities, IARC's network is closely aligned with national health bodies and academic institutions, ensuring strong support from the public sector for its initiatives.
- **Participating States as core network:** IARC Participating States form the backbone of its collaborative efforts with public organizations and contribute the largest number of Level 4 and 5 collaborators in its network. The analysis indicates IARC's effectiveness in stimulating direct research collaborations with Participating States, surpassing the level of supporting collaborations.
- **Influence of the private sector**: The private sector, primarily through not-for-profit entities, play an increasingly important role within IARC's core network, lowering public sector representation to 74% among key collaborators (Levels 3–5). Organizations such as the Bill & Melinda Gates Foundation and WCRF are pivotal in providing funding and operational expertise, which complement IARC's strong public sector partnerships.
- **Opportunities for expansion**: The analysis highlights opportunities for IARC to expand its network by collaborating with key actors in the cancer research ecosystem that are not yet part of its network. There is also potential to explore membership opportunities in countries where key collaborators are present, such as Mexico, Zimbabwe, and South Africa, as well as with other NSAs aligned with IARC's mission. Expanding these partnerships would further enhance IARC's global presence and increase its collaborative reach.

[17] https://gicr.iarc.who.int/about-the-gicr/

Annex. List of IARC key collaborators (level 3-5)

C= Scientific collaborator; F= Funder; E = Expert

Collaborators	Countries	Type of organization	Type of collab.	Level of collab.
Center for the Study of State and Society (CEDES)	Argentina	Research	C/F	3
IARC Participating State – Australia contribution	Australia	IGO/Gov	F	5
Cancer Council Victoria (CCV)	Australia	Private not-for-profit	C/E/F	4
Monash University	Australia	Research	C	3
Royal North Shore Hospital	Australia	Hospital	C/E	3
University of Melbourne	Australia	Research	C/E	4
University of Sydney	Australia	Research	C	3
Australian Ministry of Health	Australia	IGO/Gov	F	4
IARC Participating State – Austria contribution	Austria	IGO/Gov	F	5
IARC Participating State – Belgium contribution	Belgium	IGO/Gov	F	5
University of Antwerp	Belgium	Research	C	4
European Commission (EC)	Belgium	IGO/Gov	F	5
IARC Participating State – Brazil contribution	Brazil	IGO/Gov	F	5
University of São Paulo (USP)	Brazil	Research	C/E	3
A.C. Camargo Cancer Center	Brazil	Hospital	C/E/F	3
IARC Participating State – Canada contribution	Canada	IGO/Gov	F	5
University of Toronto (UofT)	Canada	Research	C/E	4
Sinai Health System Toronto	Canada	Hospital	C/E	3
Lunenfeld Tanenbaum Research Institute	Canada	Research	C	3
McGill University	Canada	Research	C/E/F	4
Princess Margaret Cancer Centre	Canada	Hospital	C/E/F	3
University of Calgary	Canada	Research	C/E	3
University of Ottawa	Canada	Research	E	3
Canadian Institutes of Health Research (CIHR)	Canada	IGO/Gov	F	3
Queens University	Canada	Research	C	3
Juravinski Hospital and Cancer Centre, Hamilton Health Sciences	Canada	Hospital	E	3
Cumming School of Medicine, University of Calgary	Canada	Research	C/E	3
University Health Network	Canada	Research	C/E/F	3
IARC Participating State – China contribution	China	IGO/Gov	F	5
Queen Elizabeth Hospital in Hong Kong SAR	China	Hospital	E	3
University of Antioquia (UA)	Colombia	Research	C	4
Charles University (CU)	Czechia	Research	C/E/F	4
IARC Participating State – Denmark contribution	Denmark	IGO/Gov	F	5

Danish Cancer Society (DCS)	Denmark	Private not-for-profit	C/E/F	4
University of Copenhagen (UCPH)	Denmark	Research	C/E	4
Aarhus University (AU)	Denmark	Research	C	4
Statens Serum Institut (SSI)	Denmark	Research	C	3
World Health Organization Regional Office for Europe (WHO EURO)	Denmark	IGO/Gov	C/F	5
Danish Cancer Institute	Denmark	Research	C	4
IARC Participating State – Egypt contribution	Egypt	IGO/Gov	F	5
IARC Participating State – Finland contribution	Finland	IGO/Gov	F	5
IARC Participating State – France contribution	France	IGO/Gov	F	5
French Agency for Food, Environmental and Occupational Health and Safety (ANSES)	France	IGO/Gov	C/E/F	4
National Research Agency (ANR)	France	IGO/Gov	F	4
National Agency for Research on AIDS and Viral Hepatitis (ANRS)	France	IGO/Gov	F	3
Paris Public Hospitals (AP-HP)	France	Hospital	C	4
Association for the Fight Against Cancer (ARC)	France	Private not-for-profit	F	4
Léon Bérard Centre (Centre Léon Bérard)	France	Hospital	C/E	4
National Cancer Institute of France (INCa)	France	IGO/Gov	F	5
Gustave Roussy (Institut Gustave Roussy)	France	Hospital	C/E	4
Curie Institute (Institut Curie)	France	Hospital	C/E	3
National Institute of Health and Medical Research (INSERM)	France	Research	C/E/F	5
Ligue Against Cancer (Ligue Contre le Cancer)	France	Private not-for-profit	F	4
General Mutuality of National Education (Mutuelle Générale de l'Éducation Nationale)	France	Private not-for-profit	F	4
French National Cancer Network (UNICANCER)	France	Research	C	5
Claude Bernard Lyon 1 University (Université Claude Bernard Lyon 1)	France	Research	C	3
Saclay University (Université Paris-Saclay)	France	Research	C	5
UPEC University (Université Paris-Est-Créteil-Val-de-Marne)	France	Research	C/E	5
INSERM - Center for Epidemiology and Population Health Research (CERPOP)	France	Research	C	3
Paris 13 University - Sorbonne Paris Nord	France	Research	C	4
European Science Foundation	France	Private not-for-profit	F	5
Endowment Fund	France	Private not-for-profit	F	4
3R - Research and Realizations	France	Research	F	4
IARC Participating State – Germany contribution	Germany	IGO/Gov	F	5
German Institute of Human Nutrition Potsdam-Rehbrücke (DIfE)	Germany	Research	C	5
Federal Ministry of Education and Research	Germany	IGO/Gov	F	4
German Cancer Aid	Germany	Private not-for-profit	F	4

German Institute of Human Nutrition Potsdam-Rehbrücke	Germany	Research	F	4
Helmholtz Association - German Cancer Research Center (DKFZ)	Germany	Research	C/E/F	5
Helmholtz Center Munich - German Research Center for Environmental Health	Germany	Research	C	3
National Center for Tumour Diseases (NCT)	Germany	Research	F	3
Heidelberg University	Germany	Research	C/E	3
University of Potsdam	Germany	Research	C	4
University Hospital of Halle	Germany	Hospital	C	3
Federal Office for Radiation Protection	Germany	IGO/Gov	F	4
German Ministry of Health	Germany	IGO/Gov	F	4
University of Augsburg Medical School	Germany	Research	F	3
University of Health and Allied Sciences, Fred N. Binka School of Public Health	Ghana	Research	C	3
University of Ioannina	Greece	Research	C	3
IARC Participating State – Hungary contribution	Hungary	IGO/Gov	F	5
IARC Participating State – India contribution	India	IGO/Gov	F	5
Public Health Foundation of India	India	Research	C	3
Rajiv Gandhi Centre for Biotechnology (RGCB)	India	Research	C/E	5
Cancer Institute WIA Chennai	India	Research	C	4
Christian Fellowship Community Health Centre	India	Hospital	C	3
GBH American Hospital	India	Hospital	C	4
Jehangir Clinical Development Centre	India	Hospital	C	4
Karkinos Healthcare Pvt. Ltd	India	Private for-profit	C	5
Nargis Dutt Memorial Cancer Hospital	India	Hospital	C	4
Tata Memorial Centre	India	Hospital	C/E/F	3
Gandhi Medical College/Tims	India	Research	E	3
IARC Participating State – Islamic Republic of Iran contribution	Iran (Islamic Rep. of)	IGO/Gov	F	5
Tehran University of Medical Sciences	Iran (Islamic Rep. of)	Research	C/F	3
IARC Participating State – Ireland contribution	Ireland	IGO/Gov	F	5
University College Dublin (UCD)	Ireland	Research	C/E	3
Irish Ministry of Health	Ireland	IGO/Gov	F	4
IARC Participating State – Italy contribution	Italy	IGO/Gov	F	5
University Hospital City of Health and Science of Turin	Italy	Hospital	C	4
Catholic University of the Sacred Heart	Italy	Research	C	3
San Paolo Company Foundation	Italy	Private not-for-profit	F	4
National Cancer Institute - IRCCS Foundation	Italy	Research	C	3
Aviano Cancer Research Institute (CRO)	Italy	Hospital	C	3
Gemelli Polyclinic Hospital	Italy	Hospital	C	3
Italian Association for Cancer Research (AICR)	Italy	Private not-for-profit	F	4

University of Florence	Italy	Research	C/E	3
University of Naples Federico II	Italy	Research	C	4
University of Turin	Italy	Research	C/E	4
IARC Participating State – Japan contribution	Japan	IGO/Gov	F	5
National Cancer Center of Japan	Japan	IGO/Gov	C/E	3
Luxembourg Ministry of Health	Luxembourg	IGO/Gov	F	3
National Institute of Public Health of Mexico	Mexico	IGO/Gov	C	5
IARC Participating State – Morocco contribution	Morocco	IGO/Gov	F	5
Cancer Association of Namibia	Namibia	Private not-for-profit	C	5
IARC Participating State – Netherlands contribution	Netherlands	IGO/Gov	F	5
Care Research Netherlands (ZON)	Netherlands	IGO/Gov	F	4
Dutch Ministry of Public Health, Welfare and Sports	Netherlands	IGO/Gov	F	4
Dutch Prevention Funds	Netherlands	IGO/Gov	F	4
LK Research Funds	Netherlands	IGO/Gov	F	4
Maastricht University	Netherlands	Research	C	3
Netherlands Cancer Registry	Netherlands	IGO/Gov	F	4
Netherlands National Institute for Public Health and the Environment	Netherlands	IGO/Gov	C/F	4
Statistics Netherlands	Netherlands	IGO/Gov	F	4
Utrecht University	Netherlands	Research	C/E	5
Netherlands Ministry of Health	Netherlands	IGO/Gov	F	5
IARC Participating State – Norway contribution	Norway	IGO/Gov	F	5
BEVITAL	Norway	Private for-profit	C	3
Norwegian Cancer Society	Norway	Private not-for-profit	F	3
Norwegian University of Science and Technology (NTNU)	Norway	Research	C	3
UiT The Arctic University of Tromsø	Norway	Research	C	4
University of Oslo	Norway	Research	C/E	4
Ministry of Public Health and Social Welfare	Paraguay	IGO/Gov	C	3
IARC Participating State – Qatar contribution	Qatar	IGO/Gov	F	5
IARC Participating State – Republic of Korea contribution	Rep. of Korea	IGO/Gov	F	5
IARC Participating State – Russian Federation contribution	Russian Federation	IGO/Gov	F	5
IARC Participating State – Saudi Arabia contribution	Saudi Arabia	IGO/Gov	F	5
Gulf Center for Disease Control and Prevention	Saudi Arabia	IGO/Gov	F	5
University of Witwatersrand	South Africa	Research	C	3
IARC Participating State – Spain contribution	Spain	IGO/Gov	F	5
Catalan Institute of Oncology (ICO)	Spain	IGO/Gov	C	4
Biomedical Research Networking Center (CIBER)	Spain	Research	C/F	5
Andalusian School of Public Health	Spain	Research	C	4

Virgen de la Arrixaca University Clinical Hospital	Spain	Hospital	C	4
Catalan Institute of Oncology	Spain	Research	C	4
Institute for Biomedical Research of Bellvitge (IDIBELL)	Spain	Research	C	4
Institute of Biosanitary Research Granada (IBS Granada)	Spain	Research	C	4
Gipuzkoa Health Research Institute	Spain	Research	C	4
Institute of Health Carlos III	Spain	Research	C/F	4
Murcia Regional Health Council	Spain	IGO/Gov	C	4
Institute of Public Health of Navarra	Spain	IGO/Gov	C/F	4
Regional Government of Andalusia	Spain	IGO/Gov	F	4
Regional Government of Asturias	Spain	IGO/Gov	F	4
Regional Government of Basque Country	Spain	IGO/Gov	F	4
Ramon Llull University	Spain	Research	C	3
University of Barcelona	Spain	Research	C	3
University of Granada	Spain	Research	C	4
University of Murcia	Spain	Research	C	3
Research Institute of the Hospital of the Holy Cross and Saint Paul	Spain	Research	C	4
Jordi Gol University Institute for Primary Care Research	Spain	Research	C	3
IARC Participating State – Sweden contribution	Sweden	IGO/Gov	F	5
County Council of Skane	Sweden	IGO/Gov	F	4
Karolinska Institutet	Sweden	Research	C/E/F	4
Lund University	Sweden	Research	C	4
Skane University Hospital	Sweden	Hospital	C	3
Swedish Cancer Society	Sweden	Private not-for-profit	F	4
Swedish Research Council	Sweden	IGO/Gov	F	4
Umea University	Sweden	Research	C/F	5
IARC Participating State – Switzerland contribution	Switzerland	IGO/Gov	F	5
Union for International Cancer Control (UICC)	Switzerland	IGO/Gov	F	4
World Health Organization (WHO)	Switzerland	IGO/Gov	C/E/F	4
European Society for Medical Oncology (ESMO)	Switzerland	Private not-for-profit	F	4
IARC Participating State – UK contribution	UK	IGO/Gov	F	5
African Cancer Registry Network	UK	Research	F	3
World Cancer Research Fund (WCRF)	UK	Private not-for-profit	F	5
Cancer Research UK	UK	Private not-for-profit	C/F	5
UK Department of Health	UK	IGO/Gov	F	3
Imperial College London	UK	Research	C/E/F	5
King's College London	UK	Research	C/E/F	4
Medical Research Council (MRC)	UK	IGO/Gov	F	5
Queens University Belfast	UK	Research	F	3
University of Bristol	UK	Research	C/E/F	4

University of Cambridge	UK	Research	C/E	4
University of Leeds	UK	Research	C	3
University of London	UK	Research	C	4
University of Manchester	UK	Research	C/E	4
University of Oxford	UK	Research	C/E	5
University of Central Lancashire	UK	Research	C/E/F	3
London School of Hygiene and Tropical Medicine (LSHTM)	UK	Research	C/E/F	4
University College Dublin School of Medicine	UK	Research	E	3
Cancerwise	UK	Private not-for-profit	F	4
Charities Aid Foundation	UK	Private not-for-profit	F	5
IARC Participating State – USA contribution	USA	IGO/Gov	F	5
Vital Strategies, Global Grants Program	USA	Private not-for-profit	F	4
Albert Einstein College of Medicine (AECOM)	USA	Research	C	3
American Cancer Society (ACS)	USA	Private not-for-profit	C/E/F	4
Baylor College of Medicine (BCM)	USA	Research	C/E/F	4
Beckman Research Institute of City of Hope (Beckman)	USA	Research	C/F	4
Bill & Melinda Gates Foundation (Gates Foundation)	USA	Private not-for-profit	C/F	5
Brigham and Women's Hospital (BWH)	USA	Hospital	C/E	4
Cancer Research Center of Hawaii (CRCH)	USA	Research	C	3
City of Hope (City of Hope)	USA	Hospital	C/E	3
Cornell University (Cornell)	USA	Research	C	4
Emory University (Emory)	USA	Research	C/E	4
Fred Hutchinson Cancer Center (Fred Hutch)	USA	Research	C/E	4
Harvard Medical School (Harvard Med)	USA	Research	C/E	3
Harvard T.H. Chan School of Public Health (Harvard Chan)	USA	Research	C	4
Harvard University (Harvard)	USA	Research	C	5
Johns Hopkins University (JHU)	USA	Research	C/E	3
Massachusetts General Hospital (MGH)	USA	Hospital	C/E	5
Mayo Clinic (Mayo)	USA	Hospital	C/E	5
Medical College of Wisconsin (MCW)	USA	Research	C/E	3
Memorial Sloan Kettering Cancer Center (MSKCC)	USA	Hospital	C/E	5
Montefiore Medical Center (Montefiore)	USA	Hospital	C	3
Neuroendocrine Tumour Research Foundation (NETRF)	USA	Private not-for-profit	F	4
NIH National Cancer Institute (NCI)	USA	IGO/Gov	C/E/F	5
Rollins School of Public Health	USA	Research	C	3
St Jude Children's Research Hospital (St Jude)	USA	Hospital	C/E	3
Stanford University (Stanford)	USA	Research	C/E	4
Susan G. Komen for the Cure Foundation (Komen Foundation)	USA	Private not-for-profit	F	3

University of California (UC)	USA	Research	C/E	5
University of Chicago (UChicago)	USA	Research	C/E	3
University of Michigan (UM)	USA	Research	C/E	3
University of Missouri (Mizzou)	USA	Research	C/E/F	4
University of North Carolina Chapel Hill (UNC)	USA	Research	C/E	3
University of Pennsylvania (UPenn)	USA	Research	C/E	4
University of Pittsburgh (Pitt)	USA	Research	C/E	4
University of South Carolina (USC)	USA	Research	C	3
University of Southern California (USC)	USA	Research	C	3
University of Utah (U of U)	USA	Research	C/E	4
University of Virginia (UVA)	USA	Research	C/E	3
University of Washington (UW)	USA	Research	C/E	4
Washington State University (WSU)	USA	Research	C	3
Weill Cornell Medicine (Weill Cornell)	USA	Research	C/E	3
Yeshiva University (Yeshiva)	USA	Research	C	3
Centers for Disease Control and Prevention (CDC)	USA	IGO/Gov	E/F	5
Stanford University School of Medicine (Stanford Med)	USA	Research	E	3
Texas Children's Hospital Baylor College of Medicine (Texas Children's)	USA	Research	E	3
University of Nebraska Medical Center	USA	Research	E	3
University of Texas MD Anderson Cancer Center (MD Anderson)	USA	Research	C/E	5
Vanderbilt University Medical Center (VUMC)	USA	Hospital	E	4
Yale School of Medicine (Yale Med)	USA	Research	E	3
US Department of Defense (DoD)	USA	IGO/Gov	C/F	3
Mark Foundation for Cancer Research	USA	Private not-for-profit	F	4
University of Zimbabwe	Zimbabwe	Research	C	4
Harare Health and Research Consortium	Zimbabwe	Research	C	4

Case studies

Inputs

- Resource mobilization and fundraising (see MTS Evaluation report, p.18)
- Data Protection (see MTS Evaluation report, p.149)
- Nouveau Centre (new headquarters) (see MTS Evaluation report, p.40)

Outputs

- Collaboration with the WHO Academy (see MTS Evaluation report, p.80)
- IARC Mutographs project (see Appendice, p.52)
- EPIC project (see Appendice, p.62)
- EpiChildCan project (see Appendice, p.73)

Outcomes

- GICR (see MTS Evaluation report, p.113)
- Global Cancer Observatory (see MTS Evaluation report, p.125)
- IARC Summer School (see MTS Evaluation report, p.106)
- Scientific IT platform (see MTS Evaluation report, p.141)
- Open access biobank and BCNet programme (see MTS Evaluation report, p.44)

Impacts

- *IARC Handbooks* programme (see MTS Evaluation report, p.198)
- *IARC Monographs* programme (see MTS Evaluation report, p.185)
- World Code Against Cancer Framework (see MTS Evaluation report, p.207)
- CanScreen5 (see MTS Evaluation report, p.220)
- ABC-DO study (see MTS Evaluation report, p.242)
- WHO Classification of Tumours (WHO Blue Books) (see MTS Evaluation report, p.227)

IARC Mutographs project

Case study

Summary

The Mutographs of Cancer project, launched in 2017 under Cancer Grand Challenges (CGC), is a pioneering global research initiative aimed at identifying the causes of cancer through the study of mutational signatures (i.e. unique DNA mutation patterns caused by various cancer-inducing factors). With a £20 million budget, this interdisciplinary effort spans 27 countries, merging genomic research with epidemiological data to uncover how environmental and lifestyle exposures induce cancer. By doing so, Mutographs seeks to improve cancer prevention strategies, reveal new therapeutic targets, and inform global public health policies. The project's name, Mutographs, reflects its goal of capturing a "picture" of cancer-causing mutations, much like a photograph, to better understand cancer development.

Initially funded for a 5-year period in 2017, the Mutographs project was extended until May 2032.

Overview of the project

Objectives and target audience

The key objectives of the Mutographs project are:

- Catalogue mutational processes driving cancer by analysing genomes across various cancer types and global populations.
- Investigate geographical and temporal variations in cancer incidence, linking mutations to environmental and lifestyle exposures.
- Develop computational tools and resources for global researchers to analyse mutational signatures.
- Support cancer prevention by identifying signatures that connect cancer to preventable exposures.

The target audience includes cancer researchers, clinicians, computational biologists, epidemiologists, public health policy-makers, and stakeholders invested in cancer prevention and treatment.

History and evolution

The Cancer Grand Challenge, "Discover how unusual patterns of mutation are induced by different cancer-causing events", was established in 2015 to address key gaps in understanding the causes of cancer. At the time, although many cancer-causing agents had been identified, substantial knowledge gaps remained, particularly concerning the mutagenic mechanisms behind many cancers. This challenge recognized the potential of analysing mutational signatures (i.e. distinct patterns of mutations caused by environmental, lifestyle, or endogenous factors).

The decline in the cost of genome sequencing and the development of computational methods enabled the large-scale deployment of mutational signature analysis. This provided an unprecedented opportunity to uncover the environmental, lifestyle, and possibly unknown carcinogenic exposures contributing to global cancer incidence. Furthermore, the team sought to investigate non-mutagenic modes of carcinogenesis, which had received less attention despite their potential importance.

Mutographs brought together cancer epidemiology and somatic genomics to create a large-scale international effort to collect cancers from various global regions, sequence their genomes, and analyse mutational signatures (see II. Structure). The project included experimental studies in

rodents and cells to support human cancer analysis and focused on computational tool development, ensuring public access to mutational signature data (see the next section). Importantly, it aimed to analyse normal tissues for somatic mutations, further illuminating the effects of carcinogenic exposure on non-cancerous tissues.

Since its inception, the project has made significant strides, evolving into a powerful collaborative network involving more than 27 countries and collecting samples from more than 8000 patients. Mutographs has used cutting-edge technologies such as NanoSeq, advanced computational tools, and high-throughput sequencing to unravel cancer mutations at a global scale.

Key successes over the years include influencing scientific thinking, identifying new mutagenic exposures, providing computational tools for mutational analysis, and establishing a rich biobank for future research. Notably, the project has also played a vital role in training researchers, sharing insights with the public, and creating patient advocacy recommendations (see III. Global reach and impact).

Along with Mutographs, the PROMINENT[18] and DISCERN[3] projects will continue focusing on new dimensions of cancer research. PROMINENT will explore non-mutagenic processes, particularly how certain carcinogens promote cancer without directly causing mutations. In addition, DISCERN will investigate how the internal and external exposome can contribute to cancer risk.

Methodology and tools

Mutographs has established a global research pipeline that spans five continents, facilitating the collection of samples and metadata from patients with cancer. This effort includes overcoming logistical and regulatory hurdles, processing samples, conducting pathology reviews, extracting DNA, sequencing, computational analysis, and distributing data to collaborators. The scale and international scope of this work are unprecedented, requiring unparalleled teamwork across global teams.

Six Work Packages (WPs) target different aspects of cancer research, including animal studies (WP3), cell culture (WP4), computational analysis (WP2), and normal tissue studies (WP5, WP6), all informed by epidemiological data and cancer genome sequencing (WP1). IARC is leading WP1 “Mutational signatures in five cancer types across five continents”.

The methodological process is detailed below:

- **Sample collection and data gathering:** Tumour and blood samples are collected from more than 8000 patients with cancer across 27 countries, focusing initially on five types of cancer with significant global variation (colorectal, pancreatic, kidney, oesophageal squamous cell carcinoma, and oesophageal adenocarcinoma). The collection has expanded to include head and neck, gall bladder, and upper urothelial cancers.
- **Epidemiological data**: Patients provide detailed lifestyle, environmental, and medical history data, which helps researchers correlate genetic mutations with potential environmental or lifestyle cancer risks.
- The project uses the **IARC Biobank**, which stores more than 100 000 biological samples, including tumour tissues, blood, and epidemiological data.
- **Whole-genome sequencing**: Samples are processed for both cancerous and non-cancerous cells. This comparison reveals specific mutational signatures associated with cancer-inducing factors.
- **Advanced sequencing technology**: Technologies such as “duplex” sequencing (NanoSeq) are used, enabling the detection of subtle mutations in cancerous and non-cancerous tissues, offering insights into how cancer-causing mutations develop over time.

[18] https://www.cancergrandchallenges.org/prominent
[3] https://discern.iarc.who.int

- **In vitro and animal studies:** Miniature, lab-grown organoids from cancerous tissues are exposed to various potential carcinogens to observe the emergence of mutational signatures. Rodent studies complement human data by exposing animals to environmental carcinogens and analysing resultant mutational signatures.
- **Computational analysis:** Tools such as SigProfiler are used to identify and categorize mutational signatures, enabling researchers to trace mutational patterns to specific carcinogenic exposures. Mutational data are mapped across the genome to highlight regions particularly affected by mutagenic exposures.
- **Data integration:** Genomic data are cross-referenced with patient metadata (demographics, lifestyle, and environmental exposures) to explore the relationship between mutational signatures and potential cancer risk factors, such as diet or carcinogens.
- **Open data sharing**: The project ensures that all findings, including genomic data and metadata, are uploaded to public repositories like the European Genome-Phenome Archive (EBI-EGA) and the Catalogue of Somatic Mutations in Cancer (COSMIC) (see III. Global reach and impact).

Structure

Governance framework

The governance framework of Mutographs is designed to ensure seamless collaboration across its international and multi-institutional partnerships, under the coordination of the Wellcome Sanger Institute in UK (project lead).

At the core is a Steering Group, which meets biannually to provide strategic oversight, review progress, and set priorities for resource allocation. This group is composed of senior scientists, institutional leads, and external advisors, ensuring that the project remains on course toward its scientific objectives while maintaining ethical and operational integrity.

Resources

Mutographs was awarded a £20 million grant by Cancer Research UK (CRUK), with the Wellcome Sanger Institute serving as PI. The funds are centrally managed by the Wellcome Sanger Institute.

Additional funding was secured through the DISCERN project (€10 million) and the PROMINENT project (€25 million).

IARC provides DNA extraction services through its biobank, and the Centre Léon Bérard (CLB) offers laser capture services.

Operational management is decentralized, with principal investigators (PIs) managing day-to-day activities for their respective WPs. Each PI leads a team responsible for executing specific research aims. These PIs meet bi-monthly through formal videoconferences to review progress, share findings, and address any obstacles in the workflow. They also hold informal meetings when necessary.

Key institutional collaborators include:

- **IARC**: Serving as the central coordinating body, IARC manages the collection, processing, and biobanking of samples and metadata from around the world.
- **Wellcome Sanger Institute**: This institute plays a pivotal role as project lead and in sequencing DNA samples collected by the project. Its computational expertise enables the large-scale analysis needed to extract and interpret mutational signatures.
- **University of California, San Diego (UCSD)**: The UCSD team leads the development of computational tools for analysing mutational signatures, including the widely used SigProfiler software.

Given the project's international scope, ethical governance is crucial, particularly regarding sample collection, patient consent, and data privacy. Local ethics committees in each participating

country review and approve these protocols to ensure compliance with both local and international standards for human research.

IARC played a pivotal role in overseeing the recruitment process for the project. It was responsible for coordinating the collection of participant data across multiple countries, ensuring that the recruitment met the ethical and logistical standards required for a large-scale international study.

International collaborative network

The success of Mutographs is grounded in its extensive collaborative network, encompassing more than 46 medical centres in 27 countries. Medical institutions in Africa, Asia, Europe, and North and South America provide the clinical samples, epidemiological data, and clinical expertise needed for the research and include:

Africa:
- Moi University, Kenya
- College of Medicine, Malawi
- Morocco Cancer Research Institute, Morocco
- University of Cape Town, South Africa
- Kilimanjaro Clinical Research Institute (KCRI), United Republic of Tanzania

Asia:
- Digestive Disease Research Institute, Tehran University, Islamic Republic of Iran
- Cancer Institute of Iran, Tehran University, Islamic Republic of Iran
- Golestan Research Center, Islamic Republic of Iran
- Tata Memorial Centre, India
- National Cancer Center, Japan
- National Cancer Institute, Thailand
- Chiang Mai University, Thailand
- Prince of Songkla University, Thailand

Europe:
- Charles University, Czechia
- Masaryk Memorial Cancer Institute, Czechia
- Palacky University, Czechia
- National Cancer Institute, Lithuania
- M. Sklodowska-Curie Institute, Poland
- Nofer Institute of Occupational Medicine, Poland
- National Institute of Public Health, Romania
- Blokhin National Medical Research Center, Russian Federation
- IOCPR, Serbia
- University of Turin, Italy
- MRC Cancer Unit, University of Cambridge, UK
- Leeds Institute of Medical Research, UK
- University Hospital Centre (UHC) Zagreb, Croatia
- National Cancer Institute, Ukraine
- Hellenic Cooperative Oncology Group (HeCOG), Greece
- Medical University of Sofia, Bulgaria

North and South America:
- Ontario Institute for Cancer Research, Canada
- Mount Sinai Hospital, Canada
- University Health Network, Canada
- McGill University, Canada

- Division of Cancer Epidemiology, National Cancer Institute, USA
- National Toxicology Program, USA
- Mayo Clinic, USA
- National Cancer Institute, Brazil
- AC Camargo Cancer Center, Brazil
- Barretos Cancer Hospital, Brazil
- Hospital de Clinicas de Porto Alegre, Brazil
- Hospital Santa Rita de Cassia, Brazil
- National Cancer Institute, Colombia
- Fundación Santa Fé de Bogotá, Colombia
- Italian Hospital, Argentina
- Institute of Oncology Angel H. Roffo, Argentina
- University of the Republic, Uruguay

In addition, ongoing collaborations with the OPTIMISTICC (Vall d'Hebron Institute of Oncology, in Barcelona) and eDyNAmiC (University of California, San Diego) teams are deepening insights into mutational signatures and extrachromosomal DNA (ecDNA). This work was published in 2022 and has led to further co-analyses and joint papers under review.

Global reach and impact

Bridging HICs innovation with LMICs access

Mutographs is built on a foundation of global cancer epidemiology, investigating five major cancer types across five continents. Through collaborations with more than 46 centres in 27 countries (see II. Structure, 2. International collaborative network), the project bridges HICs with LMICs to ensure an inclusive focus on cancer burdens across diverse populations. For example, in India and Africa, the project focuses on cancers such as oesophageal and gall bladder cancers, which show unique regional patterns.

One of the standout collaborations is with Tata Memorial Hospital in Mumbai, India. At the request of the Director of the Tata Memorial Centre, the project engaged in a pilot study on gall bladder cancer. This collaboration focused on building local capacity for mutational signature analysis, with the Sanger Institute and UCSD teams providing three tailored training sessions on SigProfiler techniques and result interpretation. A notable discovery was the unexpected presence of aristolochic acid exposure in cases of gall bladder cancer in India.

In addition, Mutographs facilitates knowledge transfer by making genomic data available to the wider scientific community through platforms like the COSMIC[19] and ICGC-ARGO[20] databases and providing open access computational tools that allow researchers worldwide to analyse mutational signatures (SigProfiler tools). The tools are available through a simple permissive licence which enables anyone to use the software[21]. This has resulted in wide adoption of the tools (see V. Key performance indicators).

[19] https://cancer.sanger.ac.uk/cosmic
[20] https://www.icgc-argo.org/
[21] https://github.com/AlexandrovLab

Influence on scientific research

The Mutographs project's findings have reshaped scientific perspectives on cancer causation and laid the groundwork for future research directions.

The project has significantly advanced scientific understanding by identifying widespread mutagenic exposures, both known and unknown. One of its key achievements is the shift in recognizing non-mutagenic (promotional) carcinogens, which play a pivotal role in cancer by enhancing the clonal expansion of cells with pre-existing "driver" mutations. Two primary types of carcinogens are now recognized:

- Mutagenic carcinogens: These increase mutation loads and trigger "driver" mutations, as observed with tobacco smoke and ultraviolet radiation.
- Non-mutagenic carcinogens: These promote the proliferation of cells with pre-existing mutations, as seen in both experimental rodent studies and human tissues.

Major discoveries in somatic mutations include:

- New "driver" mutations (FOXO1, GPAM, CIDEB) in liver cells, revealing new drug targets and patent applications for potential therapeutic interventions.
- It was found that some bronchial cells escape tobacco-induced mutations, preferentially repopulating lung tissue after smoking cessation.
- The discovery that normal breast tissues carry cancer-associated driver mutations opens up avenues for preventive strategies.
- Chemotherapy induces premature ageing in normal cells, raising concerns about long-term side-effects.
- Studies on mutation rates in normal cells challenge the somatic mutation theory of ageing.

The Mutographs project identified mutagenic exposures linked to cancers, such as aristolochic acid in clear cell renal cancer (Romania, Serbia), unknown mutagens in renal and hepatocellular cancers in Japan, and microbiome agents in early-onset colorectal cancer.

Non-mutagenic carcinogens:

- Rodent studies showed that suspected environmental carcinogens may act through promotion rather than mutagenesis.
- Oesophageal squamous cell carcinomas from diverse geographical regions showed no evidence of mutagenic exposure, supporting the role of promotional carcinogenesis.

Preparing the ground for public health policies

One of the central goals of the Mutographs project is to directly inform public health policies by elucidating how environmental and lifestyle exposures contribute to cancer development globally.

The Mutographs project has illuminated the significant role of chronic inflammation and tissue damage in cancer progression. This insight could influence global cancer prevention policies, emphasizing the management of chronic diseases and inflammation. For example, the identification of aristolochic acid as a carcinogen in Eastern Europe and Asia highlights the need for policy changes regarding traditional herbal medicines.

The discovery that normal tissues harbour precancerous mutations for years without malignancy may prompt revisions in cancer screening protocols, leading to more targeted strategies.

The Mutographs project's work on liver mutations in patients with metabolic diseases has implications for the development and stratification of new treatments, with patents already filed in collaboration with Cancer Research Horizons.

Advocacy

Mutographs has actively engaged patient advocates in its research. Advocates Maggie Blanks and Mimi McCord have participated in field trips to Kenya and Czechia, gaining insights into local cancer care and research environments. Their feedback has helped shape how health-care messages can be tailored to different communities. The observations from these interactions have been shared with researchers and the public, contributing to a more nuanced understanding of cancer prevention and communication strategies.

Mutographs has been involved in numerous public-facing activities, such as participating in the Science Museum's "Cancer Revolution: Science, Innovation, and Hope" exhibition in London. The "Cancer Detectives" activity at science festivals and the webinar "It's in the Genes" have helped to bridge the gap between science and the public.

A report on patient advocacy was compiled by Wellcome Connecting Science, offering recommendations for improving patient engagement in international research projects like Mutographs.

Interface with other Pillars and Branches

Pillar 1	Pillar 2	Pillar 3	Pillar 4
CSU: Collaboration has expanded, particularly through the use of Globocan data for colorectal cancer studies, a partnership expected to grow as additional datasets are incorporated.	**NME:** Ongoing participation as co-investigators in the PROMINENT and DISCERN projects	**ENV:** Ongoing collaborative projects in Africa focusing on the role of environmental exposures in cancer development.	**ESC**: The Mutographs team frequently uses ESC's pathology laboratories and slice scanners for histological analysis. The identification of specific sub-groups within Mutographs' findings may have direct implications for the **IARC Blue Books** classification system. There is also recognition that artificial intelligence will play a pivotal role in future **IARC Blue Books** updates, a significant area of focus for the Mutographs. **LCB:** Mutographs is involved in discussions to provide courses on genomic epidemiology, which will potentially be offered in collaboration with ESMO in the coming year.

Scientific IT platform: Mutographs has established a close collaboration with IT Services, becoming one of the largest users of the Scientific IT Platform.

IARC Biobank: The biobank plays a crucial role in the processing, storage, and management of biological samples for the Mutographs project's global studies.

Key Performance Indicators (KPIs)

The Mutographs team uses a wide range of KPIs that align with the project's overarching objectives to discover cancer-causing mutational signatures and apply them to public health improvements. The KPIs can be categorized into several broad areas:

- **Key research achievements:** The team monitors its key research achievements through detailed reporting of whole-genome sequencing across various cancer types. These milestones are systematically listed in its annual reports, providing a clear overview of the project's progress. Each report highlights significant breakthroughs, such as the sequencing of tumour and normal tissue samples from cancers including oesophageal squamous cell carcinoma, colorectal cancer, pancreatic cancer, and renal cell carcinoma (see III. Global reach and impact, 2. Influence on scientific research).

- **Publications outputs:** One of the KPIs for the Mutographs, PROMINENT, and DISCERN projects is the publication of high-impact research papers. In 2022 alone, eight papers were published, bringing the total to 47 until 2024, with five more under review. From 2023 to 2024 10 publications

- **Research resources outputs:** The project tracks the number of patients recruited and the collection of tumour and blood samples across five continents. As of the 2023 annual report, Mutographs has received tumour and blood samples from more than 8000 individuals across 46 centres in 27 countries, stored at IARC. In the past year, more than 1000 DNA samples entered the sequencing pipeline at the Sanger Institute, and data from more than 1000 additional patients was analysed and made available for epidemiological and mutational signature studies by the Mutographs team.

- **Data availability:** Mutographs tracks its contributions by releasing genomic and epidemiological data to global platforms like COSMIC, which has significantly evolved, integrating dynamic features for analysing and exploring signatures, including epidemiological and clinical associations. With more than 1 million visits and 9536 downloads in 2022, COSMIC is a widely used resource in the scientific community. The creation and improvement of tools like SigProfiler and SigFit for mutational signature analysis are also significant KPIs on data availability. These tools have been extensively used within the project and were made available to the wider scientific community.

- **Scientific training outputs:** Another KPI focuses on the number of students, postdoctoral researchers, and pathologists trained in cutting-edge techniques like mutational signature analysis. More than 75 professionals have benefited from these initiatives.

- **Advocacy outputs:** Finally, the team tracks its advocacy outputs through patient engagement and public outreach (see III. Global reach and impact, 4. Advocacy).

Alignment with IARC MTS 2021-2025

Contribution to IARC's mission

Involvement in the creation and development of collaborative networks: IARC seeks "to promote international collaboration in cancer research[22]".

➔ By establishing collaborations with 27 countries across five continents (see II. Structure), the project plays a significant role in fostering international collaboration.

Development and use of innovative methodologies: "Biological determinants of cancer will be identified by applying state-of-the-art omics profiling techniques, including metabolomics, proteomics, epigenomics, and next-generation sequencing to large-scale, population-based epidemiological cohorts.[23]"

➔ Since its inception, Mutographs has used cutting-edge technologies such as NanoSeq, advanced computational tools, and high-throughput sequencing to unravel cancer mutations on a global scale (see I. Overview of the project, 3. Methodology and tools). Mutographs has also developed and refined computational tools such as SigProfiler. These tools have advanced the ability to detect mutational signatures, contributing to the global cancer research community's capacity to understand cancer etiology on a molecular level.

Integration in the IARC Project Tree

Mutographs integrates into the IARC Project Tree by contributing to multiple strategic objectives:

- **Level 2 Objective:** The project supports Level 2 Objective #2, "Understanding the causes of cancer"
- **Level 3 Objectives:**

➔ **Objective 2.1**: "Enhance understanding of new and known causes/risk factors for human cancer, including those that accompany key cancer transitions, and those related to cancer disparities, through the conduct of epidemiological studies"

➔ **Objective 2.2:** "Enhance understanding of and elucidate biological mechanisms of carcinogenesis relevant to environmental/lifestyle factors, including those that accompany key cancer transitions, and those related to cancer disparities, through the conduct of laboratory studies".

Knowledge mobilization and capacity-building: "IARC will ensure that relevant cooperation activities are conducted in a balanced manner across all continents and regions.[24]"

➔ The Mutographs team has trained more than 75 students, postdoctoral researchers, and professionals in advanced cancer research techniques like mutational signature analysis, enhancing local expertise in both HICs and LMICs. Mutographs also promotes knowledge transfer by making cutting-edge bioinformatics tools and genomic data available through open access platforms like COSMIC and ICGC-ARGO (see III. Global reach and impact, 1. Bridging HICs innovation with LMICs access).

Achievements of assigned objectives

Continuation of the project: "The large Mutographs of Cancer project will continue, with the aim of identifying new causes of cancer through whole-genome sequencing and linking mutational signatures to possible novel cancer causes.[25]"

➔ Mutographs has processed tumour and blood samples from more than 8000 individuals across 46 centres in 27 countries. More than 1000 DNA samples entered sequencing last year, and data from an additional 1000 patients were made available for further analyses (see V. Key performance indicators).

[22] *IARC Medium-Term Strategy 2021-2025*, p. 10.
[23] *Ibid.*, p. 23
[24] *Ibid.*, p. 17
[25] *Ibid.*, p. 52.

➔ The project has significantly advanced the objective of identifying new causes of cancer through whole-genome sequencing and linking mutational signatures to potential novel cancer causes. For example, it discovered widespread mutagenic exposures like aristolochic acid in clear cell renal cancer, and unknown mutagens in Japan, providing new insights into cancer etiology across different regions. In addition, the findings have implicated microbiome-derived agents in early-onset colorectal cancer and suggested the role of "promotional" carcinogens, advancing the global understanding of cancer mechanisms and prevention strategies (see III. Global reach and impact, 2. Influence on scientific research, and 3. Preparing the ground for Public Health policies).

Main challenges and future perspectives

Challenges

Challenges with large-scale multidisciplinary, international research:

- In multi-institution teams, determining first authorship posed challenges due to significant contributions from various researchers.
- Initial project delays in recruiting and training staff were mitigated through flexible no-cost extensions. Retaining existing teams for follow-up studies became critical to avoid future delays.
- Managing paperwork across 30 countries and more than 5000 patients required significant effort, although IARC's pre-established systems helped minimize delays.
- The COVID-19 pandemic also had an impact on the project. Although the team continued data analysis, patient sample collection was delayed. Clinical teams adapted by shifting to virtual patient consent and follow-up, mitigating long-term disruption.

Perspectives

➔ Mutographs has set the stage for an ambitious future agenda to conduct a **global survey of mutational and non-mutational exposures that contribute to cancer**. This will involve genome sequencing of normal tissues on a much larger scale (thousands of individuals), revealing the factors and mechanisms contributing to cancer risk. Technologies such as advanced DNA sequencing and reductions in cost will further enable this effort.

➔ Future studies will focus on **identifying the intensity, prevalence, geographical distribution, and timing of mutagenic exposures**. This will entail significantly larger, geographically diverse studies. In addition, research will aim to uncover unknown agents responsible for these exposures, such as the enigmatic mutagenic signatures discovered in Romania, Serbia, and Japan (see III. Global reach and impact, 2. Influence on scientific research).

➔ Mutographs has revealed that many human carcinogens may act through non-mutagenic mechanisms. Future research will monitor **driver mutation clones in normal tissues** to identify how non-mutagenic carcinogens promote cancer development. This will be central to ongoing projects such as PROMINENT and DISCERN (see I. Overview of the project, 2. History and evolution).

➔ Discoveries from Mutographs suggest that mutated clones in metabolic disease-related genes (e.g. FOXO1, GPAM) offer protection against disease toxicity. This approach could lead to the **identification of new drug targets for treating systemic diseases and mitigating their effects on organs like the liver**.

➔ Future research will focus on **the long-term effects of chemotherapy on normal tissues**. Somatic mutation landscapes will be studied across large patient populations treated with various chemotherapies, offering insights into therapeutic choices, side-effects, and long-term biological consequences. This could help improve cancer treatment strategies and better predict treatment-related side-effects.

- The project will continue to **release valuable datasets**, including genomic and clinical metadata, to global platforms like ICGC-ARGO and EBI-EGA[26]. These resources will provide the scientific community with access to comprehensive data for future cancer research, enhancing global collaboration and extending the impact of Mutographs findings.
- The legacy of Mutographs includes **continued curation of mutational signatures in the COSMIC database and ongoing improvements to computational tools like SigProfiler**. This will ensure that reference signatures remain updated, enabling new discoveries in cancer genomics well beyond the project's conclusion.

For more details

- Mutographs project website
- PROMINENT project website

[26] https://ega-archive.org/

EPIC
Case study

Summary

EPIC is a large-scale cohort study that focuses on the relationship between diet, nutrition, lifestyle, and environmental factors in the development of cancer and other chronic diseases. It is one of the largest cohort studies worldwide, encompassing more than 521,000 participants from 10 European countries. Over its >30 years of follow-up, EPIC has accumulated one of the largest biobanks globally, including millions of biological samples. The cohort now includes more than 62,000 cancer cases, making it a powerful resource for studying disease etiology.

The study has made significant contributions to understanding the links between diet, lifestyle, metabolic factors and the risk of cancers and other chronic conditions. EPIC findings have influenced public health policies and continue to provide valuable evidence on the benefits of healthy lifestyles for disease prevention.

Overview of the project

Objectives and target audience

The European Prospective Investigation into Cancer and Nutrition (EPIC) was designed to study the complex interactions between diet, nutrition, and lifestyle factors and their effects on risk of cancer risk and other chronic diseases. EPIC aims to identify risk factors and protective factors that can guide cancer prevention strategies, benefiting public health at both the population and individual levels.

The study targets researchers, public health professionals, and policymakers to provide evidence-based recommendations for cancer prevention.

History and evolution

EPIC began in the 1990s as a collaborative initiative among independent European cohorts. The goal was to establish a unified infrastructure that would enable large-scale, cross-country studies on the relationship between diet, cancer, and chronic diseases in diverse populations. The project focused on three key components:

- **Biobank creation:** Most participating centres provided biological samples (serum, plasma, DNA) from all participants, with the exception of Scandinavian centres. These efforts helped to establish the IARC biobank, which now holds more than 6 million samples, including a significant proportion for EPIC.
- **Common variables:** Harmonization work between countries ensured that data on diet, lifestyle, and other variables were comparable across all centres, allowing for consistent analysis.
- **Census tools:** A uniform questionnaire was developed to capture detailed dietary and lifestyle information, including food classification and 24-hour dietary recalls, facilitating standardization across diverse populations.

Coordinated by IARC, the project received support from the European Commission, which helped lay the groundwork for the study.

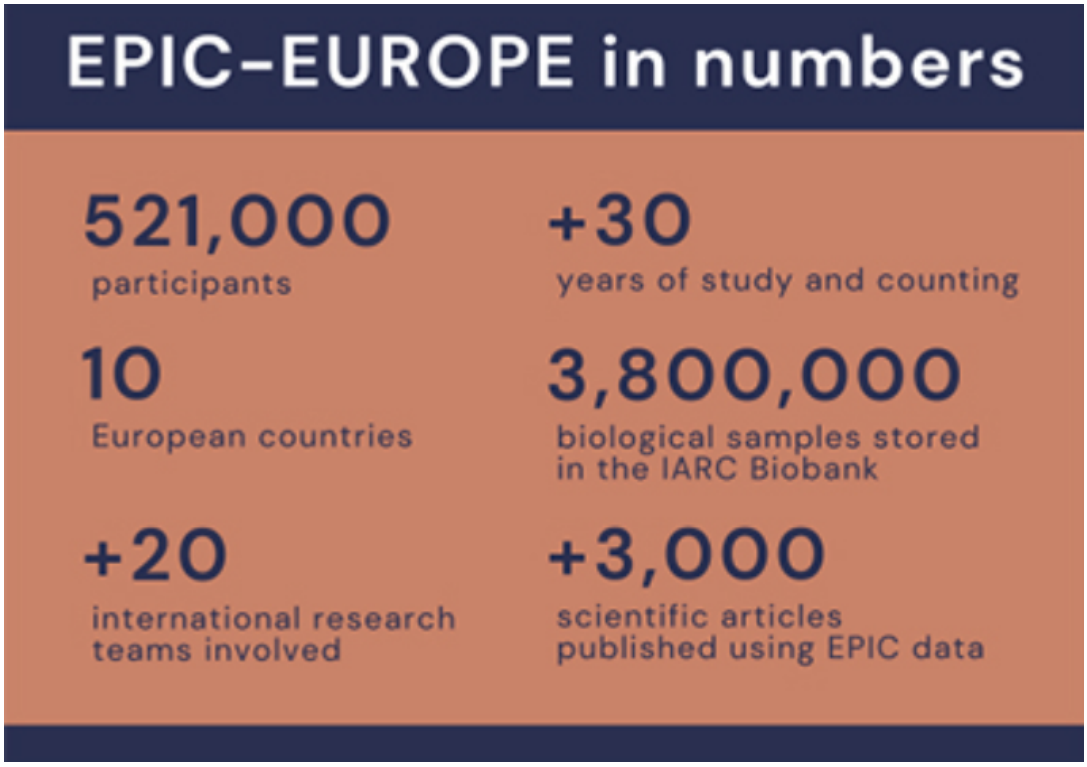
EPIC has periodically updated follow-up data every 5-10 years, tracking participant outcomes such as cancer and chronic disease incidence. However, recent challenges, including the GDPR, local resource constraints, and the COVID-19 pandemic, have delayed data updates. There are ongoing efforts to address the administrative and logistical hurdles needed to keep the database

current. Updating this database remains the cohort's top priority (see VIII. Main challenges and future perspectives).

EPIC stands out due to its size, its scope, and the detailed exposure information and biospecimens it collects. Over the past 25 years, more than half a million participants have provided data, contributing to one of the largest collections of incident cancer cases globally.

While EPIC initially concentrated on cancer mortality, it expanded to include broader health outcomes, such as cardiovascular diseases, diabetes, and multimorbidity. The cohort has grown significantly, with more than 74 000 participants diagnosed with cancer as of 2016, alongside 15 000 cases of type-2 diabetes and 24 000 cardiovascular events. EPIC's large dataset also allows for the study of rarer cancers, such as kidney, pancreatic, and ovarian cancers. This expansion is reflected in additional projects, such as the EPIC InterAct Project (which investigates type-2 diabetes risk factors) and the EPIC CVD Project (which studies cardiovascular disease risks).

EPIC's molecular research has also progressed with the integration of genome-wide association studies (GWAS) and targeted metabolomics. More than 57,000 EPIC participants now have available GWAS data, enabling deeper analyses of genetic and molecular factors contributing to cancer and chronic diseases.



EPIC key numbers[1].

Methodology and tools

EPIC's methodology is founded on a prospective design, meaning that data are collected before the onset of diseases, offering unique insights into the factors that lead to illness.

Participants were recruited from 10 European countries (Denmark, France, Germany, Greece, Italy, the Netherlands, Norway, Spain, Sweden, and the UK) in 1993 and 1999, providing a diverse population with varying dietary habits and disease patterns. In total, 521,457 healthy adults, primarily aged 35–70 years, were enrolled across 23 centres, with recruitment spanning countries

such as Denmark (11%), France (14%), Germany (10%), Greece (5%), Italy (9%), the Netherlands (8%), Norway (7%), Spain (8%), Sweden (10%), and the UK (17%). Notably, the Oxford centre in the UK recruited 27,000 vegetarians and vegans, creating the largest study subgroup of this dietary population.

	Male	Female	Number of participants
EPIC-Europe	153 425	367 898	521 323

Dietary intake was assessed through country-specific dietary questionnaires tailored to capture local food habits. Common 24-hour diet recalls were collected on a sample of 8% of EPIC participants to strengthen dietary harmonization. Participants also provided lifestyle information, including smoking and alcohol consumption and physical activity. In addition, data on reproductive history and medical history were collected. Anthropometric measurements, such as body mass index (BMI) and waist-to-hip ratio, were recorded at recruitment. These data provide key information on participants' physical characteristics, which are essential for studying links between body composition and disease.

A significant strength of the EPIC study lies in its collection of biological samples, which includes blood samples collected from approximately 400,000 participants. These samples are processed into plasma, serum, white blood cells, and erythrocytes, and stored in liquid nitrogen at -196°C in IARC's biobank. This biobank allows for future biomarker, genetic, and biochemical studies, making it a valuable resource for investigating cancer and other chronic diseases.

EPIC follows up participants over time, with repeat interviews and questionnaires every 3-5 years to assess changes in diet, lifestyle, and health status. Cancer outcomes and mortality data are regularly updated, providing a long-term, comprehensive dataset. Two approaches are used for follow-up: active follow-up, where participants are contacted directly, and passive follow-up, linking centre data with national cancer registries.

Although most of the data focuses on dietary and lifestyle determinants, the study also includes specific projects like the GenAir case-control study, which investigates the effects of passive smoking and air pollution on cancers and respiratory diseases.

Structure

Governance Framework

EPIC is coordinated by IARC, the Nutrition and Metabolism Branch (NME) is responsible for managing EPIC's infrastructure, which includes the centralization of data on cancer outcomes, lifestyle, diet, anthropometric measurements, and molecular data. IARC, with its extensive biobank, also hosts and maintains the master EPIC database. This database includes information collected from participating centers across Europe. Imperial College London jointly oversee the project.

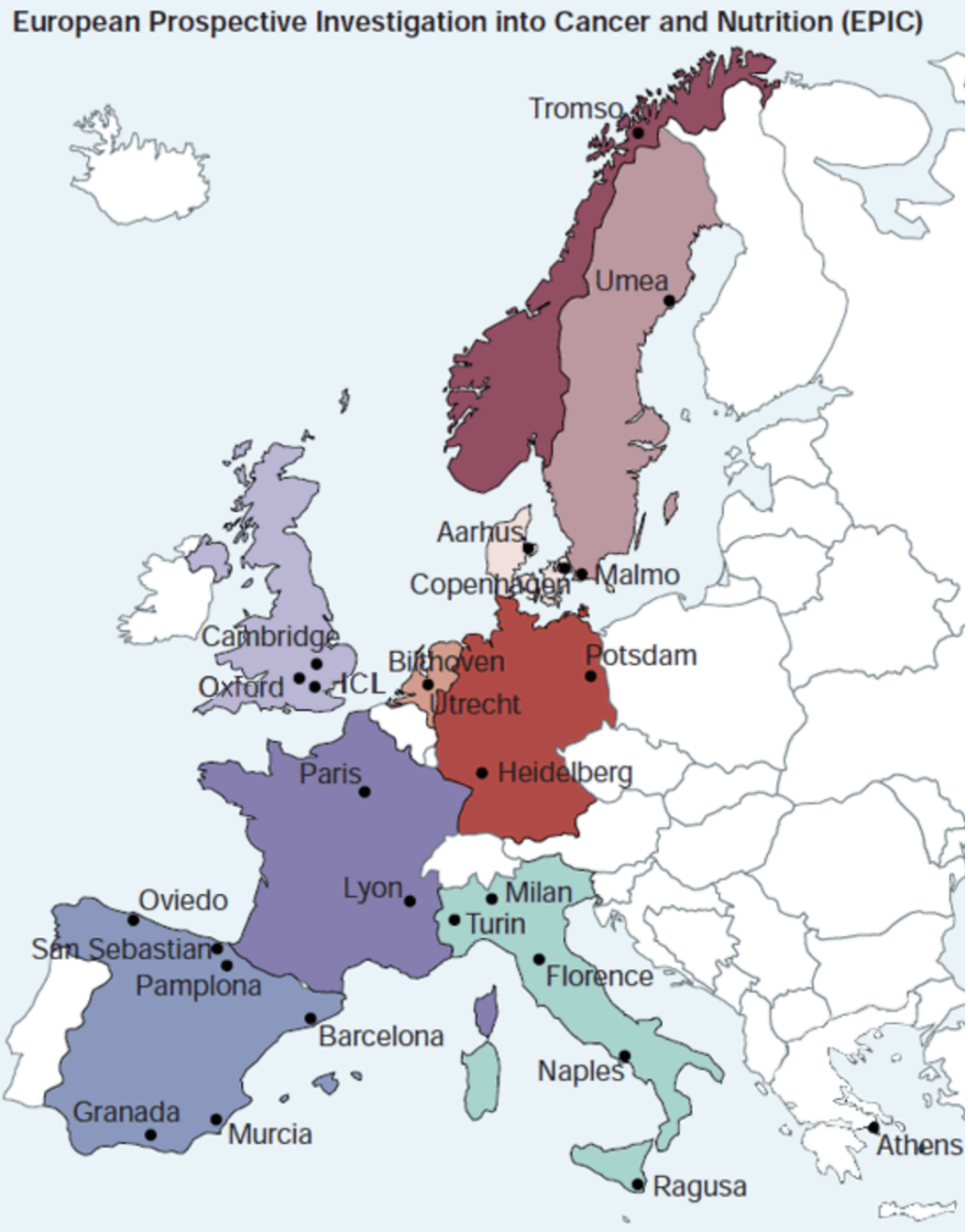
The EPIC-Europe Steering Committee oversees the project's activities. Comprised of principal investigators from all EPIC cohorts, the committee holds regular meetings to review new scientific ideas, approve research projects, and manage resources. Decisions are made by consensus, and the committee meets once a month via teleconference, with annual in-person meetings.

EPIC research is organized into specialized Working Groups that focus on key areas of research, such as diet and cancer, biomarkers, and genetics. These groups propose new projects, which are reviewed and approved by the Steering Committee.

International collaborative network

A significant strength of EPIC is its broad geographical coverage, involving multiple European countries. Each country contributes to the research by investigating diet and cancer, as well as chronic diseases, within its population:

- **EPIC-Oxford (UK)**: The Oxford cohort consists of 57,500 participants, focusing on the dietary habits of vegetarians and vegans, examining the influence of diet on cancer and other chronic diseases.
- **EPIC-Norfolk (UK)**: Based at the University of Cambridge, this cohort includes 25 639 participants. It collects detailed data on lifestyle, diet, physical activity, and socioeconomic status, alongside biological samples.
- **Netherlands**: Two research centers in Bilthoven and Utrecht contribute to EPIC. The cohorts were merged in 2006-2007 to create EPIC-NL, enhancing sample size and data efficiency.
- **Denmark**: The Diet, Cancer and Health study recruited 57,053 participants in 1993-1997. It focuses on diet, lifestyle, and cancer development, with detailed biological samples collected and stored.
- **France**: EPIC-France is derived from the E3N-Generations cohort, which includes about 140 000 participants. The initial E3N cohort of nearly 99 000 women has been actively followed up since 1990.
- **Germany**: EPIC participants were recruited from Potsdam (27,548) and Heidelberg (25,540), with a focus on understanding how lifestyle and diet contribute to chronic diseases.
- **Italy**: Several Italian cohorts from Florence, Naples, Turin, and Ragusa are part of EPIC. These cohorts study diet and cancer, particularly focusing on the regional dietary habits of central and southern Italy.
- **Norway**: The Norwegian Women and Cancer Study (NOWAC) became part of EPIC in 2000, expanding EPIC's focus to northern Europe with 37 200 women.
- **Spain**: EPIC-Spain involves five regions (Asturias, Basque Country, Gipuzkoa, Murcia, and Andalucía) and contributes 41 437 participants.
- **Sweden**: The Malmö Diet and Cancer Study and the Västerbotten Intervention Project (VIP) are Sweden's main contributions to EPIC, involving tens of thousands of participants.



EPIC principal investigators and collaborating centres[2].

Resources

EPIC is funded by a combination of European and national sources. Major funders have been and still include:

- **European Commission**: Through the "Europe Against Cancer" programme.
- **IARC and Imperial College London**: Provide critical coordination and infrastructure support. The National Institute for Health and Care Research (NIHR) also supports EPIC through Imperial College.

The national cohorts receive support from various local agencies, including:

- **Denmark** : Danish Cancer Society
- **France** : Ligue Contre le Cancer, Institut Gustave Roussy, Mutuelle Générale de l'Education Nationale (MGEN), Institut National de la Santé et de la Recherche Médicale (INSERM), French National Research Agency (ANR), French Ministry for Higher Education

- **Germany**: German Cancer Aid, German Cancer Research Center (DKFZ), German Institute of Human Nutrition Potsdam-Rehbrüecke (DIfE), Federal Ministry of Education and Research (BMBF)
- **Italy**: Associazione Italiana per la Ricerca sul Cancro-AIRC-Italy, Italian Ministry of Health, Italian Ministry of University and Research (MUR), Compagnia di San Paolo
- **The Netherlands**: Dutch Ministry of Public Health, Welfare and Sports (VWS), The Netherlands Organisation for Health Research and Development (ZonMW), Netherlands Cancer Registry (NKR), World Cancer Research Fund (WCRF)
- **Norway**: UiT The Arctic University of Norway; Health Research Fund (FIS)
- **Spain**: Health Research Fund (FIS), Instituto de Salud Carlos III (ISCIII), Regional Governments of Andalucía, Asturias, Basque Country, Murcia, and Navarra, Catalan Institute of Oncology - ICO
- **Sweden**: Swedish Cancer Society, Swedish Research Council and County Councils of Skåne and Västerbotten
- **United Kingdom**: Cancer Research UK, Medical Research Council

Data generation for EPIC is primarily funded through competitive grants from organizations such as the WCRF, INCa, NIH, and the European Commission, although attempts to secure cohort or infrastructure-specific funding have been less successful. NME has been proactive in securing direct funding and grants for several recent projects from agencies like the French National Research Agency (ANR), the L'Oréal Foundation, and Imperial College London (see VII. Alignment with IARC MTS 2021-2025, 2. Achievement of assigned objectives).

At IARC, a core team of about 10 individuals, including several technicians, is involved in supporting EPIC, although not all are dedicated to the project full-time. These staff members are funded through the regular budget (RB), which ensures the ongoing maintenance and coordination of the study.

Global reach and impact

Impact on public health policies and guidelines

EPIC has significantly advanced scientific research and public health across Europe. With more than 521 000 participants from 10 countries, EPIC provides a vast dataset that has driven important discoveries about cancer risk factors, dietary habits, and chronic diseases. These findings have equipped governments and public health officials with evidence to shape policies aimed at preventing cancer and other chronic conditions.

By 2004, more than 26 000 new cancer cases were documented among participants, with breast, colorectal, prostate, and lung cancers being the most common. Subsequent analyses, focusing on various cancer types, have expanded knowledge about the genetic factors, hormonal influences, and dietary components that contribute to cancer risk.

Key findings from EPIC data have resulted in the publication of more than 3000 scientific papers.

Some important results from 2008 include:

- ➔ Lower sodium intake from salt and higher potassium intake from fruits and vegetables promote healthier blood pressure levels.
- ➔ High physical activity, particularly involving weight-bearing exercises, is linked to increased longevity and a reduced risk of bone fractures.
- ➔ A diet rich in dietary fiber significantly protects against bowel cancer.
- ➔ Obesity raises the risk of various types of cancer.

- Elevated levels of sex hormones are associated with a higher risk of breast cancer.
- High fat intake increases the likelihood of developing breast cancer.
- Greater consumption of fruits and vegetables is linked to a lower risk of death from all causes.
- Elevated blood glucose levels correlate with an increased risk of heart disease.
- The combined effect of four healthy behaviours-not smoking, staying physically active, consuming alcohol in moderation, and eating at least five servings of fruits and vegetables daily-can extend life expectancy by up to 14 years.

Further research in 2012 and 2013 found that:

- Dietary flavonoid intake is associated with a reduced risk of gastric carcinoma in women, but not in men.
- Regular consumption of processed meat increases the risk of cardiovascular diseases and cancer-related mortality.

By 2021, additional findings showed that:

- Dietary factors such as raw vegetable intake, dietary fiber, and adherence to the Mediterranean diet were linked to lower cancer mortality. Other beneficial dietary patterns included those followed by low meat eaters, vegetarians/vegans, or fish eaters.

The impact of EPIC's research extends beyond academia, influencing nutrition guidelines, public health policies, and even consumer behaviour. For example, the EPIC study played a key role in the development of the Nutri-Score, a front-of-package food labeling system designed to guide consumers toward healthier choices. Researchers from IARC, the Nutritional Epidemiology Research Team (EREN) in France, and other partners found that people who regularly consume foods with lower nutritional quality (as indicated by a lower Nutri-Score) have a higher likelihood of dying earlier from all causes compared with those who consume foods with higher nutritional quality (as indicated by a higher Nutri-Score). This study, published in the *British Medical Journal*, used data from more than half a million participants in EPIC.

Interface with other Pillars and Branches

EPIC plays a crucial role in fostering collaboration across various IARC Pillars and Branches, and its data are widely used for research purposes. Given its vast dataset on diet, lifestyle, and other health factors, EPIC serves as an essential resource for multiple Branches within IARC:

Pillar 1	Pillar 2	Pillar 3	Pillar 4
CSU relies on EPIC data to support research projects, particularly in the analysis of cancer incidence, survival, and mortality trends.	**GEM** is a key collaborator on the EPIC study, contributing to genomic and molecular analyses of cancer risk factors. GEM scientists use EPIC's biobank to conduct genome-wide association studies (GWAS) and other genetic studies that investigate the links between genes and cancer development.	**ENV:** EPIC data have been instrumental in shaping the recommendations of the ECAC, particularly by informing the identification of key lifestyle and environmental determinants of cancer. NME scientists led the nutrition working group for the ECAC programme and provided recommendations on obesity, physical activity, diet, alcohol consumption, and breastfeeding.	In the **ESC** Branch, **IHB** collaborates with NME on projects related to nutrition and obesity. NME collaborates with **IMO** on scientific workshops related to bias impact and chemoinformatics approaches.

		EGM uses EPIC data for childhood cancer and breast cancer projects. **EPR** exploits EPIC data to inform early detection strategies, particularly in cancers like breast cancer and colorectal cancer.	
IARC Biobank is highly integrated with EPIC's infrastructure. About two-thirds of the IARC biobank consists of EPIC samples, making it a crucial resource for researchers. **The Scientific IT Platform** is crucial for processing and storing EPIC data.			

Key Performance Indicators (KPIs)

EPIC uses a range of KPIs to monitor its success and impact. These include:

Scientific output and publications:
- **Number of peer-reviewed publications:** EPIC has produced more than 3000 scientific papers. EPIC is a cornerstone of IARC's research portfolio, with 9% of IARC publications linked to this cohort.
- **Citations:** The impact of EPIC research is measured by how frequently its papers are cited in other scientific work.

Participant engagement and data collection:
- **Number of participants:** EPIC recruited more than 521 000 participants across 10 European countries, and participant follow-up remains a crucial measure.
- **Follow-up rates:** Regular updates on participant health outcomes, including cancer incidence and mortality, are essential for maintaining the study's relevance.

Biospecimen collection and use:
- **Biobank samples:** The number of biological samples collected (e.g., blood, plasma, serum, DNA) and used in molecular analyses. EPIC has collected more than 9 million biospecimens, which are regularly analyzed for various biomarkers.
- **Use of biobank resources:** The extent to which stored biospecimens are used in cutting-edge research, such as biomarker discovery and genetic studies.

Collaborative projects and grants:
- **Number of international collaborations:** EPIC collaborates with numerous research centers, making its global partnerships a key measure (see II. Structure, 2. International collaborative network).
- **Grant funding secured:** Success in securing competitive grants from bodies like the European Commission, national health research bodies, and international organizations is a crucial indicator of EPIC's financial sustainability and research capacity. During the 202-2024 period, NME has undertaken a total of 34 projects. Among these, NME has directly coordinated 13 projects and successfully secured funding for 10 of them, achieving a grant success rate of 19%. Moreover, NME has received direct funding for 3 of its projects.

Alignment with IARC MTS 2021-2025

Contribution to IARC's mission

Involvement in the creation and development of collaborative networks: "IARC will increasingly partner with relevant regional organizations to further advance high-quality diagnostic practice for cancer pathology and research."

- EPIC is a prime example of IARC's commitment to building collaborative networks. The EPIC cohort, spanning over 30 years and involving 10 European countries, exemplifies IARC's ability to develop extensive partnerships and collaborative research efforts across Europe (see II. Structure, 2. International collaborative network).

Impact on the development of public health policy, national or international guidelines or recommendations: Positioning IARC "as a leading authority on global cancer prevention research"

- More than 30 years of investment in EPIC has resulted in a vast dataset on cancer risk factors, nutrition, and chronic diseases. EPIC's findings have influenced national and international public health guidelines, nutrition policies, and cancer prevention strategies, such as the development of the Nutri-Score, a food labelling system now used in several European countries. (see Global reach and impact).

Integration into the IARC Project Tree

The EPIC study integrates into the IARC Project Tree by contributing to multiple strategic objectives, particularly under Level 2 Objective:

- **Level 2 Objective:** EPIC supports **Level 2 Objective #2,** "Understanding the causes of cancer"

Level 3 Objectives:

- **Objective 2.1:** "Identify and quantify the impact of environmental, nutritional, genetic, and lifestyle factors on cancer risk."
- **Objective 2.2:** "Strengthen research on the role of modifiable risk factors, such as nutrition and physical activity, in cancer prevention."
- **Objective 2.3:** "Develop methods and tools to better measure exposure to cancer risk factors."
- **Objective 2.4:** "Expand molecular epidemiological research to understand the interaction between genetic, molecular, and environmental factors in cancer."

Achievements of assigned objectives

Understanding the causes of cancer: "Understanding the causes: Biological determinants of cancer will be identified by applying state-of-the-art -omics profiling techniques, including metabolomics, proteomics, epigenomics, and next-generation sequencing to large-scale, population-based epidemiological cohorts."

- EPIC has integrated biomarker, metabolomics, and genomics data, developing pipelines to ensure data comparability across studies. NME led several metabolomics projects using EPIC's biorepository, resulting in high-impact publications. This work includes profiling metabolites associated with cancer risk, identifying biomarkers related to diet, and investigating the genetic and metabolic factors that contribute to cancer development.

Study the role of obesity and metabolic dysfunction in cancer development: "IARC will study the role of obesity and metabolic dysfunction in cancer development, identify biomarkers of diet and nutrition and their application to cancer etiology, and investigate multimorbidity and biological pathways common to cancer, diabetes, and cardiovascular diseases, by applying its laboratory and biostatistical expertise to large-scale, population-based cohorts, such as the EPIC cohort."

- EPIC's data is central to numerous NME projects focused on obesity, metabolic dysfunction, and their links to cancer. Major projects have explored metabolomics profiling in relation to cancer, revealing important biomarkers and metabolic pathways linked to dietary habits and cancer risk. A variety of studies have examined factors such as red meat consumption, coffee

intake, and gut microbiota, contributing significantly to our understanding of how lifestyle and dietary factors influence cancer risk.

➔ Notable efforts during the 2021-2024 period include the EPIC4ND study, funded by the French National Research Agency (ANR), which focuses on predicting Alzheimer's, Parkinson's, and ALS using methylome profiling. Another major project, funded by Imperial College, investigates circulating proteins as biomarkers for cancer, diabetes, cardiovascular, and neurodegenerative diseases, using advanced SomaScan technology to analyze ~29,000 EPIC plasma samples. This research aims to identify novel biomarkers for disease risk and early detection. In addition, a project funded by the L'Oréal Foundation is studying breast cancer causes through metabolomic profiling.

Main challenges and future perspectives

Challenges

- **Impact of GDPR on data sharing:** One of the significant challenges EPIC currently faces is the implementation of the GDPR across the European Union. Data sharing regulations between EPIC centers, external collaborators, and IARC have become more stringent. Specifically, Norway, Denmark, and Sweden have encountered legal obstacles that hinder data sharing, despite scientific interest. IARC has invested in a Data Protection Officer and a Scientific IT platform to address these issues, but ongoing high-level discussions are still required to resolve compliance with GDPR.

- **Biospecimen replenishment and data centralization:** Due to GDPR and local resource limitations, replenishment of biospecimens and updates to the EPIC biobank have been suspended. In addition, planned centralization of cancer and vital status endpoint data at IARC has faced delays, despite being critical for ongoing research.

- **Ageing cohort and need for new participants:** The ageing of the EPIC cohort presents another challenge. Efforts are being made to recruit offspring of participants, enabling intergenerational studies. However, maintaining the cohort's relevance requires new participants and continued data updates.

- **Local dynamics and cohort expansion:** Maintaining momentum at local centres is another challenge, with no plans to integrate new countries into the EPIC study. Resource limitations at the local level further complicate the situation, making sustained engagement critical.

- **Funding and resources:** EPIC is a core resource for NME and relies on continuous external funding to maintain its competitive edge, including the centralization of cancer end-points, vital status, and dietary data collected during follow-up.

Perspectives

➔ **Role of nutrition and modifiable factors in cancer:** EPIC will continue to explore the role of nutrition and lifestyle in cancer development, focusing on novel biomarkers using untargeted metabolomics techniques. Projects on alcohol's role in cancer, molecular impacts, and mechanisms will continue. A new research programme with the WCRF will focus on linking diet and cancer mechanisms, informing public health recommendations.

➔ **Molecular data integration and large-scale studies:** The accumulation of molecular data offers new opportunities for large-scale epidemiological studies. Plans are in place to centralize new cancer endpoint and vital status data, as well as molecular and follow-up data on diet and lifestyle. Replenishment of the IARC EPIC biobank will be undertaken. These

resources will enable more complex analytical frameworks to exploit increasingly rich datasets, ensuring that EPIC continues as an international research leader.

- **Cancer multimorbidity research:** Investigating cancer multimorbidity, particularly the intersection of cancer and cardiometabolic diseases like diabetes and cardiovascular disease, will be a priority. EPIC will leverage existing metabolomics and proteomics data to assess shared risk factors and metabolic dysfunctions. This will be expanded through collaborations with other cohorts, including UK Biobank and NCI Cohort Consortium.

- **Research on early-onset colorectal cancer:** EPIC will initiate a programme to study rising rates of early-onset colorectal cancer. This project will seek to uncover the underlying causes of increased incidence among younger individuals, contributing to preventive strategies.

For more details

- EPIC website
- History of EPIC
- EPIC key findings

EPiChildCan

Case study

Summary

Research on childhood cancer was recognized as an IARC priority at the Scientific Council meeting in January 2019 and as a priority by WHO, which launched, in collaboration with St. Jude Children's Research Network, the first Global Initiative for Childhood Cancer (GICC) in September 2018.

In this framework, the EPiChildCan programme stands as a pioneering research initiative aiming to uncover the molecular origins of cancers in children and adolescents. The programme investigates how early-life exposures—environmental, biological agents, dietary, and lifestyle factors—alter the epigenome and contribute to cancer development. EPiChildCan also seeks to identify epigenetic markers that can serve in cancer risk prediction, early detection and prognosis, and potentially inform preventive or therapeutic interventions.

Overview of the project

Objectives and target audience

The EPiChildCan project pursues several overarching goals aimed at understanding and combating childhood cancer. Its specific objectives include:

- Identify neonatal epigenomic biomarkers of cancer risk and of "intermediate" phenotypes that predispose to later onset of cancer.
- Characterize epigenetic precursors of childhood cancer in relation to early-life exposures and "intermediate" phenotypes.
- Test the stability and potential reversibility of the early epigenetic changes in postnatal development and investigate whether such epigenetic effects persist in target tumour tissues at and after diagnosis.
- Investigate the mechanisms and functional relevance of epigenetic markers of exposure and cancer risk using integrative-omics (which relate methylation to RNA expression, mutations, and cancer driver potential) and using experimental models (eg. mouse and organoids, with highly controllable experimental settings).

The target audience includes cancer researchers, oncologists, geneticists/epigeneticists, public health professionals, paediatric cancer associations and global cancer organizations. A special emphasis is placed on knowledge-sharing across both HICs and LMICs to ensure broad applicability of the study's findings.

History and evolution

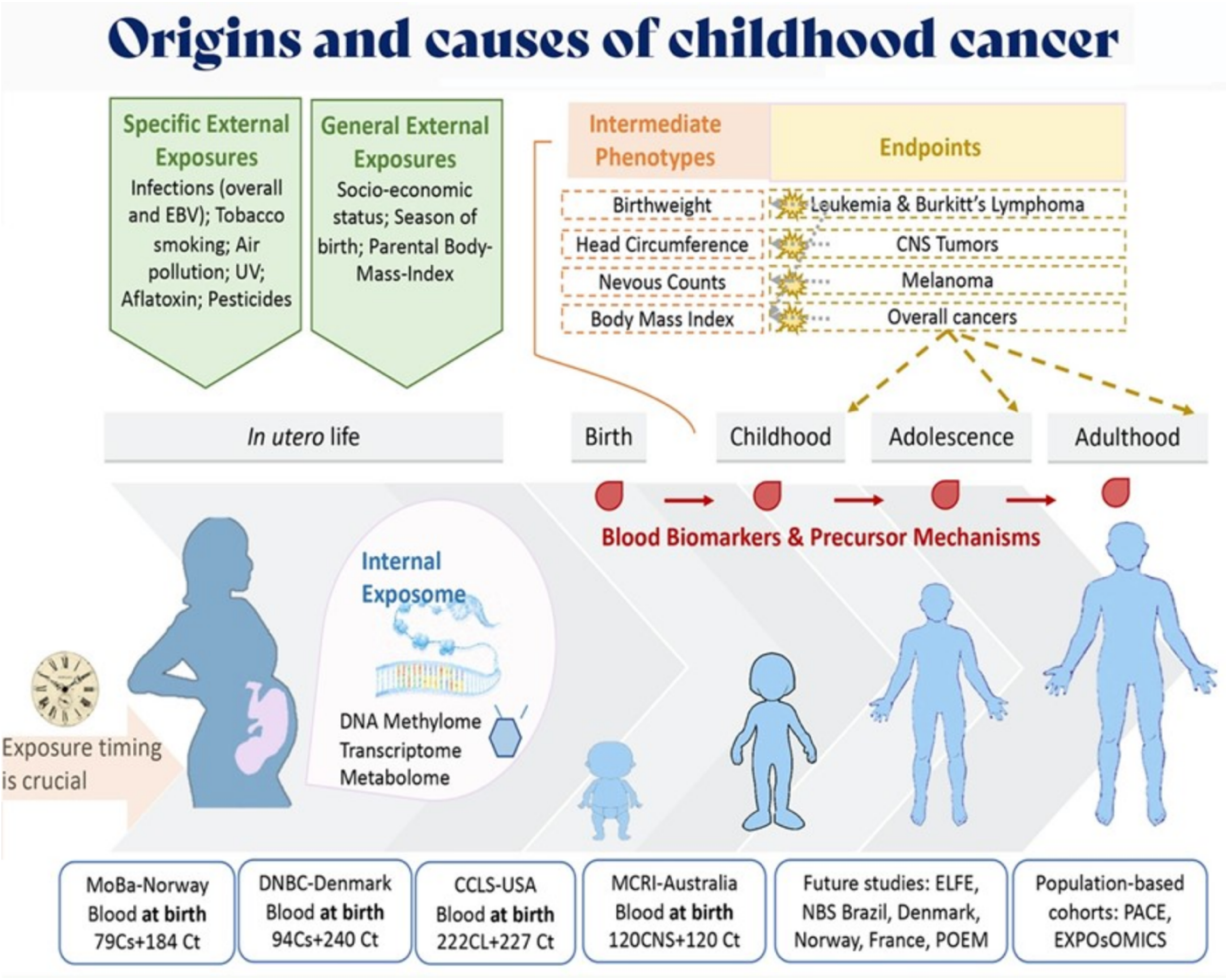
The EPiChildCan project builds on years of foundational work in epigenetics and cancer research, led by IARC's Epigenomics and Mechanisms Branch (EGM).

The project began in 2009 as a collaboration between IARC and Melbourne's Murdoch Hospital, exploring the role of the epigenome in childhood cancer, which constituted the first feasibility project of The International Childhood Cancer Cohort Consortium (I4C). Over time, this initiative expanded into a large international collaboration encompassing multiple scientific disciplines.

EGM has played a key or leading role in establishing significant international consortia, including:

- The International Childhood Cancer Cohort Consortium (I4C),
- The EpiEARLY network,
- The EXPOsOMICs consortium,
- The Aflatoxin and Epigenetics in The Gambia project,
- Pregnancy And Childhood Epigenetics (PACE)

This network of collaborations, underpinned by cutting-edge advancements in laboratory methodologies, has enabled the development of a comprehensive framework for exploring the exposome, the entirety of internal and external exposures influencing cancer risk from birth to death. The EPiChildCan project's multi-dimensional approach merges this international collaboration with the latest molecular biology, bioinformatics, and biostatistics techniques to probe the early-life origins of childhood cancer.



The hypothetical model of origins and cause of childhood cancer.

Methodology and tools

The EPiChildCan project leverages a global network of leading international consortia to investigate the molecular causes of childhood cancer, with a focus on epigenetics (see above). These consortia provide access to large, prospective datasets and biospecimens, collected before and after the onset of cancer, allowing EGM to study early-life molecular changes that predispose children to cancer and affect their survival.

A significant tool in this research is neonatal blood spots, routinely collected in several countries and linked to national cancer registries. By analyzing these blood spots, EGM identifies epigenetic changes that precede cancer development. Accordingly, EGM has accessed neonatal blood spot data from the California Childhood Leukemia Study (USA), which is part of the retrospectively designed CLIC, and identified epigenetic precursors of childhood cancer that were comparable with those observed in prospectively collected neonatal blood from I4C (Ghantous et al, Molecular Cancer 2024).

EGM is expanding this approach to include neonatal blood spots linked to cancer registries and/or to measured exposure factors, in HICs and LMICs, including geographical representation of North

and South America, Europe, Africa, Australia and Asia. Many of those regions are underrepresented in I4C and CLIC and are needed to increase the statistical power, ethnic diversity, and robustness of the findings.

EGM employs also analyses of in-house and publicly available multi-omics datasets including single-cell multi-omics to identify epigenetic precursors and drivers of childhood cancers and their link to environmental exposures specific to HICs and LMICs.

Three ongoing projects led by EGM under the EPiChildCan initiative are highlighted in this methodology as illustrative examples:

➔ **EpiLeuk Project:**

- The EpiLeuk project investigates the causal relationship between in utero and early-life exposures and the risk of childhood cancer, specifically focusing on paediatric leukaemia. A key hypothesis is that epigenetic regulation—particularly DNA methylation—plays a central role in mediating the effects of environmental, dietary, and lifestyle exposures during fetal development, influencing cancer risk later in life.

- The study uses a hybrid retrospective and prospective hybrid approach to investigate epigenetic alterations associated with paediatric leukaemia. The main focus is on identifying DNA methylome signatures that precede the onset of cancer, providing molecular precursors detectable at birth, long before the disease manifests.

- The project integrates cutting-edge methodologies for genome-wide profiling of epigenetic alterations and their interplay with gene expression, focusing on DNA methylation changes linked to childhood leukaemia risk and prognosis. These profiles are analyzed using state-of-the-art bioinformatics pipelines that EGM has developed in-house.

➔ **EpilEarlyCNS project**

- The EpilEarlyCNS project project addresses paediatric central nervous system (CNS) tumours, the most common solid tumours in children and a leading cause of cancer-related childhood deaths. Despite improvements in other childhood cancers, survival rates for CNS tumours remain low, with treatments often leading to severe side effects, including secondary cancers.

- The study investigates the largely unknown causes of these tumours, focusing on epigenetic changes, especially DNA methylation, as potential precursors. It hypothesizes that early-life epigenetic alterations are critical to understanding tumour origins, possibly beginning in utero, when cells are most susceptible to epigenetic influences. The project aims to uncover biomarkers that signal paediatric brain tumour risk, offering potential targets for early detection and therapeutic intervention.

- Due to the rarity of paediatric CNS tumours, the study uses a novel retrospective approach, analyzing both tumour samples from diagnosis and neonatal biospecimens (blood spots, cord blood) to identify early-life epigenetic changes. This approach minimizes reverse causality bias and enables a comprehensive look at the molecular landscape of brain tumours from birth onward.

- The project also uses a multi-omics approach (epigenetic, genetic, transcriptomic) including profiling of tumour samples and patient-derived cellular model combined with state-of-the-art mechanistic analyses to identify epigenetic drivers and markers of these paediatric tumours (i.e. Diffuse intrinsic midline gliomas).

➔ EpiBurkitt project

- The EPiBurkitt project aims to investigate the combined effects of Epstein-Barr Virus (EBV) infection and mycotoxins including aflatoxin B1 (AFB1) exposure on the development of Burkitt lymphoma and explore how these exposures may alter the epigenome of children in sub-Saharan Africa.

- The project employs a multi-pronged approach that includes global DNA methylation analysis of early-life collected blood spots and paediatric Burkitt lymphomas, multi-infection analyses (oncogenic viruses and parasites), cellular models, and in vivo studies to understand how exposure to EBV and mycotoxins such as AFB1 impacts the epigenome, immune system and response to other infectious agents in children and contributes to the development of Burkitt lymphoma.

Structure

Governance Framework

The EPiChildCan project is under the leadership of IARC's EGM Branch.

Key contributors to the EPiChildCan project draws on expertise and international collaborators from five continents: Australia, Europe (e.g. Norway, Denmark, Sweden, UK, France, Belgium), Asia (e.g. Lebanon, Qatar, Saudi Arabia), North and South America (e.g. USA, Canada, Brazil) and Africa (e.g. Gambia, Burkina Faso, Malawi, Kenya, United Republic of Tanzania), with additional focused varying by research area.

Links with WHO

EPiChildCan aligns with the WHO GICC, which aims to increase the global survival rate of children with cancer to at least 60% by 2030. The WHO initiative is focused primarily on treatment, and the EPiChildCan complements this approach by providing critical research and data to enhance prevention strategies.

EGM also co-leads with CSU the Childhood Cancer Awareness and Research Evidence (CCARE) team, with collaborations across IARC Pillars, including several Branches (EGM, CSU, NME, ENV, EPR and ESC).

International collaborative network

The success of EPiChildCan is driven by a robust network of international collaborations that span multiple continents. Key collaborative networks include:

- International Childhood Cancer Cohort Consortium (I4C): The largest platform for prospective data and biospecimens collected before the development of childhood cancer. IARC serves as the International Biospecimen Coordinating Centre.
- Childhood Cancer and Leukemia International Consortium (CLIC): A retrospective consortium focused on data and biospecimens collected after diagnosis. This collaboration allows the project to access crucial neonatal blood spots for comparison of epigenetic precursors across populations.
- Pregnancy And Childhood Epigenetics (PACE) and EXPOsOMICS consortia: These consortia provide additional data from population-based birth cohorts.
- The PEDIAC programme, involving INSERM and IARC, focuses on understanding the origins and causes of paediatric cancers.
- The South-Rock Consortia involving INSERM, CNRS and local universities and cancer hospitals in Lyon and Marseille in France and focuses on improving paediatric cancers prevention and treatments.
- The newly established consortia (CICERO project) between EGM, ENV, Princess Maxima Centre in the Netherlands, and local hospitals in Kenya, the United Republic of Tanzania and Malawi aims to establish cohorts in these African countries.

Resources

The EPiChildCan project is supported by multiple grants and funding agencies. The ongoing projects presented in the previous section are funded as follows:

- **EpiLeuk:** Funded by several sources, including INCa-PEDIAHR with a total budget of €150,000 allocated entirely to IARC; INCa-PEDIAC, with a total budget of €3,700,000, of which €613,376 is designated for IARC; Netherlands Ministry of Health, Welfare, and Sport with a total funding of €1,998,055 allocated to IARC; WCRF with a total budget of £346,624, including £43,024 for IARC; Children with Cancer UK Postdoctoral Fellowships, each awarded €74,000; and regular budget support from EGM.

- **EpiBurkitt:** Supported by Plan Cancer France (€306,335), the Bill & Melinda Gates Foundation (US$319,491), and contributions from the Research Foundation – Flanders (€47,000), Institut National du Cancer (INCa), and the PEDIAC consortium, with €343,396 allocated for IARC. Additional support comes from the Fondation ARC pour la Recherche sur le Cancer and Children with Cancer UK for a postdoctoral fellowship, with ongoing support from EGM's regular budget.

- **EpiEarlyCNS:** Funded with €409,806 from the French INCa and with €500,000 (€150,000 to EGM) from the European Science Foundation (ESF, Fight Kids Cancer grant).

- The French INCa has funded additional projects under the EPiChildCan umbrella. These include South-ROCK (2023-2028), an integrated center of excellence in paediatric oncology research based in southern France (Lyon and Marseille), dedicated to developing therapeutic strategies and exploring environmental factors in cancer prevention, and CICERO (2023-2025), which focuses on advancing research on childhood cancer in Africa.

Global reach and impact

Focus on LMICs

The EPiChildCan project holds significant potential for LMICs, particularly by enhancing understanding of childhood cancer's early-life risk factors.

Through studies like EpiLeuk and EpiBurkitt, the project is expanding LMIC population coverage and knowledge of the environmental and genetic factors that contribute to childhood cancer, such as the interactions between EBV, mycotoxins as AFB1 and other oncogenic viruses and parasites. This research has unveiled how these exposures impact early-life epigenetic markers, providing an evidence base for cancer prevention that is directly relevant to populations in LMICs. Identifying children at high risk through early biomarkers will reinforce primary prevention strategies and risk stratification.

EGM is also contributing its expertise in childhood cancer to collaborative projects like the CICERO project, which specifically focuses on LMICs. CICERO aims to address critical gaps in understanding the occurrence, presentation, risk factors, and prognosis of childhood cancers in these regions.

Through multiple projects, EPiChildCan continues to contribute to the training of postdoctoral and PhD researchers from various LMICs. This includes training in state-of-the-art laboratory and in silico tools and in critical skills that are transferrable to LMICs (e.g. data science, scientific writing, literature and database mining).

In addition, the involvement in the WHO GICC, in partnership with St. Jude Children's Research Network, reinforces the EPiChildCan's focus on implementing actionable interventions in LMICs.

Impact on public health policies and guidelines

EPiChildCan's research is based on a model where environmental exposures (both general and specific) and internal biological processes may induce stable and heritable changes in the epigenome. These changes can alter gene expression in stem and progenitor cells, potentially leading to childhood cancers, cancer-predisposing phenotypes, and increased cancer risk later in life. EPiChildCan has identified DNA methylation markers for a range of exposures, including specific factors like tobacco smoke, air pollution, ultraviolet radiation, aflatoxin and infections, as well as general exposures, such as socioeconomic status, season of birth, and parental BMI.

This programme has demonstrated significant potential to impact public health. For example, AHRR methylation has become one of the best biomarkers of cigarette smoking during pregnancy, superseding in various ways the well-known cotinine, and this epigenetic marker has been validated across multiple birth cohorts in one of the largest studies to date (co-led by EGM). By using advanced epigenomics and bioinformatics, this programme has also identified early-life environmental exposures, such as aflatoxin, air pollution, and infections, and their links to epigenetic changes in children that predispose them to leukaemia. For example, the imprinted VTRNA2-1 gene was identified as a key epigenetic marker at birth, linked to the risk of pre-B acute lymphoblastic leukaemia (pre-B ALL).

The translational impact of the EPiChildCan project is profound, because these research findings are not only advancing scientific knowledge but also paving the way for early risk assessment and actionable targets for both prognosis and intervention. Collaborative efforts with large international consortia (such as I4C, CLIC, PACE, and EXPOsOMICS) as well as with associations focusing or covering childhood cancer (such as Imagine for Margo and AMALOUNA) are ensuring that the findings from EPiChildCan are widely shared and integrated into global cancer prevention frameworks.

Interface with other Pillars and Branches

EGM collaborates extensively on childhood cancer research with several other IARC Branches through multiple projects:

Pillar 1	Pillar 2	Pillar 3	Pillar 4
CSU: Collaborations on childhood cancer projects such as the CICERO and South-ROCK projects.	**GEM:** Collaboration on the technology and pipelines for all projects.	**ENV:** Collaboration on CICERO, PEDIAC and PEDIAHRG projects.	**ESC:** Collaboration with the CCARE team on childhood cancers.
In addition, EGM is co-leading with CSU the IARC's **Childhood Cancer Research Team (CCARE) Team**, which is dedicated to advancing knowledge and improving outcomes for childhood cancer worldwide. The CCARE Team includes 21 team members from six IARC branches (CSU, NME, ENV, EGM, EPR, and ESC) working together with support from the Director's Office.			

Key Performance Indicators (KPIs)

The KPIs used by the EPiChildCan team are as follows:

➔ **Research and scientific impact:**

- Number of specific early-life and in utero risk factors associated with childhood cancer development.

- Number of intermediate phenotypes linked to childhood cancer risk identified through epigenetic studies.
- Epigenetic biomarkers for diagnosis, risk stratification, early detection, and potentially preventive strategies.
- Biomarkers or models developed to predict treatment outcomes or prognosis in childhood cancer.
- Number of countries involved in collecting neonatal blood spots and paediatric tumours through national registries (including less-represented LMICs countries).

➔ **Resources and knowledge sharing:**

- Total grant funding secured.
- Number of publications in peer-reviewed journals, including high-impact and specialized journals.
- Number of ECVSs involved and trained in the project, including those from LMICs
- Number of international scientific conferences, symposiums, or invited lectures attended and presentations given.
- Development of accessible content, including educational videos, and their views or reach metrics (e.g., YouTube dissemination).

Alignment with IARC MTS 2021-2025:

Contribution to IARC's mission

Involvement in the creation and development of collaborative networks: "IARC will increasingly partner with relevant regional organizations to further advance high-quality diagnostic practice for cancer pathology and research."

➔ The EPiChildCan project has built a strong, global network of collaborative partnerships to support high-quality research for childhood cancer (see II. Structure).

Knowledge mobilisation and capacity-building: "IARC is well placed to develop appropriate and tailored capacity-building programmes and to identify the most relevant target audiences for training or mentoring activities."

➔ By facilitating specialized training programmes, workshops, and mentorship opportunities, EPiChildCan has bolstered scientific capacity across partner institutions, particularly in LMICs. This includes funding for four postdoctoral researchers from LMICs (one in Kenya, one in Lebanon and two in Brazil), as well as support for two PhD candidates (including one from Brazil). In addition, three ECVSs returned to their home countries after completing their tenure at IARC, bringing enhanced expertise to their local institutions.

➔ EPiChildCan has been highlighted globally through several presentations and communications. Keynote lectures were delivered at major conferences in Houston and Tours, and invited lectures included prestigious forums such as the Princess Takamatsu Symposium in Tokyo, Baylor University, Chapel Hill, and the IUTOX Continuing Education Congress in Hawaii. In addition, EPiChildCan's findings were showcased in the late-breaking research session at the AACR Annual Meeting in Florida.

➔ To further expand reach and dissemination, a short film about EPiChildCan was produced and made available in 11 languages on YouTube.

Achievements of assigned objectives

Advancing the understanding of early-Life and in utero risk factors in childhood cancers: "IARC will enhance the understanding of molecular causes of cancers in children and adolescents driven by risk factors specific for in utero and early life, such as maternal and paternal age, adiposity during pregnancy, smoking, and alcohol consumption. IARC will also examine risk factors for second cancers and produce guidelines for registries on reporting second primary tumours in young patients."

- During the MTS period, the EPiChildCan project made substantial strides in early-life epigenetic research on childhood cancer through multiple key projects, including EpiEarly, EpiLeuk, and EpiBurkitt (see I. Overview of the project). These initiatives have expanded knowledge on how early-life exposures contribute to cancer risk, laying groundwork for new preventive strategies and biomarkers for early detection (see III. Global reach and impact).
- In addition, the EPiChildCan team actively participated in numerous scientific meetings throughout the MTS period, furthering the dissemination of project findings and fostering collaboration within the international research community.
  - Science Forum – Integrated Childhood Cancer Research for Prevention; Topic: Identifying in utero origins and epigenetic markers of childhood cancer
  - PEDIAC Consortium Annual Meeting; Topic: Epigenetics, pesticides, and childhood cancer
  - Young Global Leaders Meeting; Topic: Searching for Origins of Childhood Cancer: Mapping the "Molecular Diary"
  - BTEC Conference on Paediatric Brain Tumours; Topic: Epigenome deregulation and the origin of childhood brain tumours
  - PEDIAC Meeting on Causes and Origins of Childhood Cancer; Topic: Pesticides, Epigenetics, and Childhood Cancer
  - South-ROCK Project Kick-Off Meeting on Paediatric Cancer; Topic: Epigenetics, Interdisciplinarity in Childhood Cancer Research
  - South-ROCK Consortium Retreat; Topic: Epigenetics, predisposition, and environmental causes of childhood cancer
  - React4Kids National Congress; Topic: Identifying Epigenetic Precursors of Childhood Cancer
  - International Childhood Cancer Cohort Consortium (I4C) – Organizer and Speaker; Topic: Childhood cancer epigenomics
  - Brazilian National Cancer Institute; Topic: Childhood cancer epigenomics
  - 5th Congress of the French Society of DOHaD (Developmental Origins of Health and Disease); Topic: Early-Life Factors and Epigenetic Precursors of Childhood Cancer
  - University of Hasselt; Topic: Childhood Cancer Cross-Omics
  - University of Montpellier – Molecular Basis of Hematological Malignancies; Topic: Origins of Childhood Leukemia and Molecular Insights

Integration into the IARC Project Tree

EPiChildCan is integrated into the IARC Project Tree under the following objectives:

Level 2 objective: The project supports Level 2 objective #2, "Understanding the causes of cancer."

Level 3 objectives:

- Objective 2.2: " Enhance understanding of and elucidate biological mechanisms of carcinogenesis relevant to environmental/lifestyle factors, including those that accompany key cancer transitions, and those related to cancer disparities through the conduct of laboratory studies"
- Objective 2.3: " Enhance understanding of exposure sources, including those related to key cancer transitions, and those related to cancer disparities, and related pathways"
- Objective 2.4: " Enhance understanding of potential risk factors, including those that accompany key cancer transitions, and those related to cancer disparities, in underresearched populations and/or in LMICs and their interplay with the observed cancer patterns"

Main challenges and future perspectives

Challenges

- Epigenetic changes, including DNA methylation, are highly sensitive to environmental exposures during pregnancy and early in life, a critical period for assessing cancer risk. However, childhood cancers are rare, posing significant challenges for large-scale prospective studies. Consequently, international collaborations and innovative (including hybrid retrospective-prospective) approaches are essential.

- EPiChildCan depends heavily on external funding and grants, which are inherently unstable. This may affect key operational areas:
    - Specialized staffing: Shortages in staff with omics data analysis expertise.
    - Laboratory platform maintenance: Expensive resources to sustain cutting-edge laboratory facilities and platforms.
    - Project management: Limited resources to manage complex administrative tasks, legal frameworks and project coordination, particularly within the highly international dimension of the programme.

Perspectives

- ➔ IARC will continue to study epigenetic markers and mechanisms linked to in utero and early-life exposures and cancer predisposition. The Agency will further explore specific epigenetic changes related to shared modifiable risk factors, such as lifestyle and diet, in a multidisciplinary effort to identify biomarkers that inform cancer prognosis and risk management.

- ➔ Upcoming research will include a focused examination of pesticide exposure and endocrine disruptors. For instance, upcoming PEDIAC meetings will address endocrine disruptors, and both PEDIAC and the South-ROCK project will explore exposures in various human and mouse models, investigating potential treatment responses and resistance clusters.

- ➔ IARC will continue its efforts in studying epigenetic markers and mechanisms specific to paediatric cancers in LMICs.

- ➔ Building on findings from leukaemia studies, there is now a need to expand research into other childhood cancers, such as central nervous system (CNS) tumours and glioblastomas.

- ➔ IARC will continue to actively participate in the WHO GICC, relying on its competitive advantage based on solid scientific expertise, innovative methodological approaches, and access to unique cohorts, including those from LMICs.

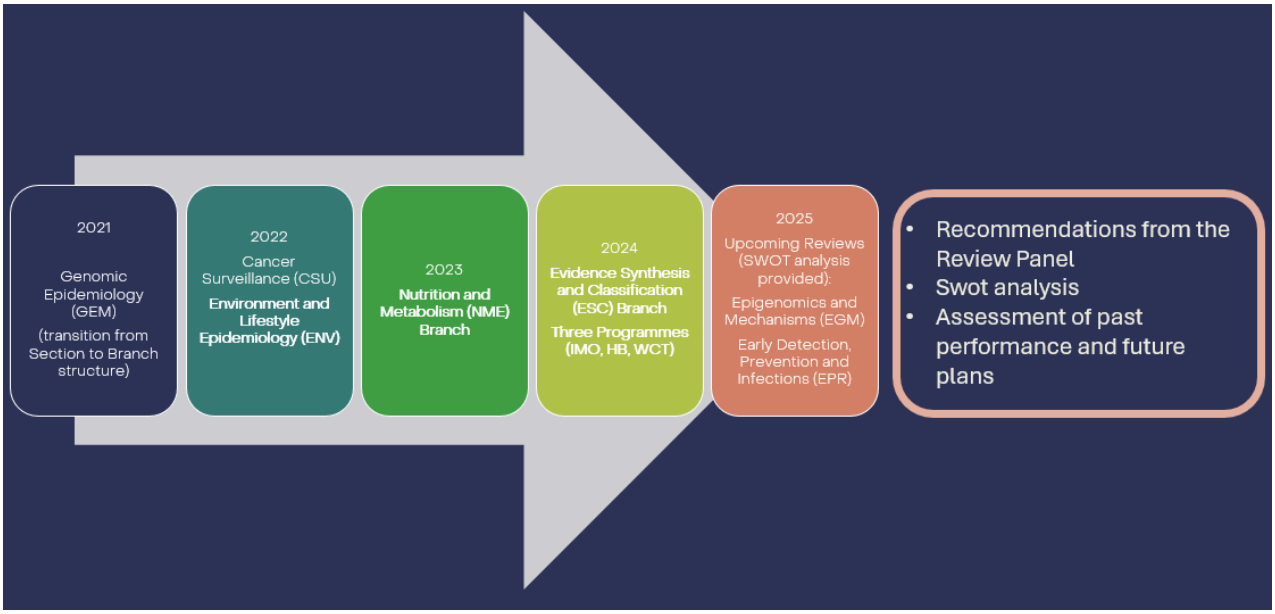
For more details

- ➔ EPiChildCan website
- ➔ EPiChildCan in video
- ➔ WHO GICC
- ➔ CCARE webpage

Branch Reviews: overview

During the MTS period, four IARC Branches underwent review, as follows:

- **2021:** GEM (formerly the Genomic Epidemiology Section), comprising the Genetic Epidemiology Group (GEP) and the Genetic Cancer Susceptibility Group (GCS).
- **2022:** CSU
- **2023:** NME
- **2024:** ESC (includes three programmes: the IARC Monographs Programme (IMO), the IARC Handbooks Programme (IHB), and the WHO Classification of Tumours Programme (WCT); the Branch was reviewed in its entirety).



Genomic Epidemiology (GEM) Review (2021)

Recommendations from the Review Panel:

- ➔ Continued support of GEM at the highest level for its proposed comprehensive research programme, training, and capacity-building, which is critical for the IARC MTS.
- ➔ Focus research strategy on addressing understudied cancers and populations, particularly in LMICs, with a high priority for research in African populations.
- ➔ Maintaining infrastructure critical to GEM and various other IARC Branches – including biobanking, pathology, bioinformatics, and novel omics technologies– is essential. At the same time, outsourcing other laboratory work, such as large-scale sequencing, should be considered where appropriate.
- ➔ GEM has overlapping interests with other Branches. Less clear was how GEM will strategically interact with other Branches, and where new opportunities might exist.
- ➔ GEM involvement and leadership in the Computational Biology, Bioinformatics, and Biostatistics Working Group is seen as critical for future GEM research (as well as IARC overall).
- ➔ The lung cancer work (early detection biomarkers) highlights cross-agency collaborations and may generalize to other early detection work within GEM (oropharyngeal cancer, bladder cancer).
- ➔ Leveraging GEM expertise as part of IARC's education programme should be enhanced.

S.W.O.T analysis

Genetic Epidemiology Group (GEP):

Strengths

Strong Group of early career Professional staff, with a range of skills, coming from diverse backgrounds.
Dedicated and experienced support staff.
Extensive network of international partners.
Successful history of raising substantial external funding through competitive grant applications, with substantial funding guaranteed through 2022–2023.
Diverse range of projects covering both primary and secondary prevention, and across a range of cancer sites.

Weakness

Unexpected loss of key staff could have a substantial disruptive effect on multiple projects.

Opportunities

Finalization of whole genome sequencing for 5000 cancers across 5 cancer sites within Mutograph project. Along with collection of clinical data, will allow for extensive additional genomic studies for these cancer sites.
Additional early detection and prognostic studies based on the extensive GEP biorepository.

Threats

Majority of external funding comes from small number of organizations, including NIH, Cancer Research UK and European Commission.
Majority of key staff are on external budgets.

Genetic Cancer Susceptibility Group (GCS):

Strengths

Established group of motivated and productive researchers with complementary research expertise, backed by important technical capabilities in laboratories and scientific IT systems.
These researchers lead a portfolio of research projects built on the opportunities available to IARC and orientated towards IARC's goals.
These research projects are productive in terms of competitive research funding and scientific outputs in peer-reviewed journals.
We are also centrally placed among many communities at IARC, allowing us to foster research activities across the Agency.

Weakness

A broad mandate of scientific research projects and responsibilities in capacity building within the Agency relative to the resources available to the Group.

Opportunities

Important opportunities for the application of GCS multi-disciplinary genomic projects to achieve IARC's research goals.
GCS researchers occupy leadership positions within collaborative networks to collect the biological materials necessary for these samples, as well as having access to the biological resources housed at IARC.
As GCS and GEP merge to form the "GEM" Branch, this should allow for further capturing the synergies between the two Groups, the "Cancer causes" pillar, and interactions with other groups, particularly through IARC's move to the "Nouveau centre".

Threats

An ageing laboratory infrastructure and expanding demands for scientific IT capacity, requiring technical upgrades.
Management risks regarding adoption of the branch model.
Limitations in meaningful career advancement for GCS staff within the UN system.
Disruption to scientific functions related to the movement of GEM into the "Nouveau centre".
The physical separation of laboratory activities from the remainder of GCS.
Maintenance of competitive research funding within increasingly capricious research funding setting.
Complications regarding the EU's GDPR laws for data sharing projects.

Assessment of past performance and future plans

The Branch was reviewed as Groups for the past performance and as a Branch for the future plans, as below:

Past performance

GEP (Group)

Assessment of GEP's scientific quality: **Outstanding**

Assessment of the relevance of GEP's work to the mission of IARC: **Perfect fit**

Past performance

GCS (Group)

Assessment of GCS's scientific quality: **Outstanding**

Assessment of the relevance of GCS's work to the mission of IARC: **Perfect fit**

Future plans

GEM (Branch)

Assessment of GEM's scientific quality: **Outstanding**

Assessment of the relevance of GEM's work to the mission of IARC: **Perfect fit**

Cancer Surveillance (CSU) Branch Review (2022)

Recommendations from the Review Panel:

- CSU is underfunded: ensure secure support (RB funding) for CSU and GICR to maintain IARC's position as a premier provider of global cancer surveillance and descriptive epidemiology research.
- Strategic positioning relative to other large international descriptive (cancer) epidemiology efforts would be valuable for CSU.
- Direct application to cancer data capture: connect CanReg5 with DHIS2 and other facility-based data platforms.
- Investigate options that maximize efficiency and collaboration in the development of PAF and other key indicators for cancer prevention.
- The multi-partner approach to estimating the proportion of cancers attributable to lifestyle and environmental risk factors in France might provide a template for country engagement.
- Cancer inequalities and Health Economics and Cancer need continued attention and support.
- New areas of research: methods for integration and harmonization of complex diverse data sources; artificial intelligence and machine learning; methods for causal inference; federated data analysis methods or synthetic data methods.
- Development of tools for the local analysis of our global data resources with national partners.
- Direct assessment of policy uptake (policy impact tools such as Overton).

S.W.O.T analysis: Cancer Surveillance (CSU) Branch

Strengths

CSU activities core to IARC's mission – reputation is strong and long-standing
Strong commitment and broadening expertise of CSU staff
GLOBOCAN 'leading brand' – GCO becoming so, related papers highly-cited
GICR is the delivery mechanism for building registry capacity in LMIC
Active registry networks through CI5-XI, SURVCAN, IACR and GICR
CSU research – output, diversity, quality and impact are all increasing
Cohesive links between all CSU activities: programmes of work, not individual projects
Increased communication of CSU brand through social media (e.g. *#GCO365*)
Continuity planning underway within Branch – from data collection to dissemination

Weaknesses

Limited core staff: around 15 for over a decade
Reliance on external funding for core activities such as registry support (GICR)
Reliance on external funding for research/indicator expansion – staff turnover
Many unfunded and expanding mandates
Key staff close to retirement – need for succession planning
Some CSU projects isolated and inefficient – need to centralize data delivery
Timeliness of online registry data on CSU websites

Opportunities

IARC comparative advantages – trust and interest in IARC across many stakeholders
Emerging areas within CSU (social inequalities/economics) prioritized in MTS
Longstanding remit from WHO to collate/disseminate cancer data
Build on links with WHO, IAEA, and other UN Agencies, etc.
High-level policy commitments to NCDs and cancer
Large research/registry networks keen for collaboration (among IARC Participating States)
Potential new partners as CSU diversifies (e-learning, AI, IT, biostats, etc.)
Pandemic has rekindled interest and need for global surveillance data
Harnessing new technologies to support registries (timeliness of data)
Prospects of communicating our work to new audiences via social media

Threats

Competitive grants increasingly difficult to attain
Reduced direct funding post-pandemic
IARC regular budget funding limited yet increasing demands
Data protection/confidentiality: a complex landscape to navigate that risks draining resources
COVID-19 pandemic continues – impact on GICR model, funding
Limited engagement with IARC Participating States – outdated governance model

Increasing administration within IARC/WHO (DTA/FENSA, etc.)
Often tenuous connections with WHO-HQ in interconnected areas of work
Crowded space: competition in all areas, particularly global estimates development
Current resource requirements to furnish Nouveau Centre
Future policies at IARC
The rise of 'real-world' non-population-based approaches to surveillance

Assessment of past performance and future plans

Past performance

CSU

Assessment of CSU's scientific quality: **Outstanding**

Assessment of the relevance of CSU's work to the mission of IARC: **Perfect fit**

Future plans

CSU

Assessment of CSU's scientific quality: **Outstanding**

Assessment of the relevance of CSU's work to the mission of IARC: **Perfect fit**

Environment and Lifestyle Epidemiology (ENV) Branch Review (2022)

Recommendations from the Review Panel:

- ➔ Internal funding from the Regular Budget be allocated to ENV.
- ➔ To increase the work being initiated and conducted in LMICs and expand it to other countries.
  - New: oil industry (Nigeria)
  - Consortium of exposures in mining industry in Africa
  - Occupational cancers in the Islamic Republic of Iran
  - Improving breast cancer survival – two new countries: Ghana, Egypt. One new activity: increasing breast awareness (Ghana, United Republic of Tanzania)
  - Recent additional activity – skin cancer in persons with albinism
  - Codes Against Cancer – LAC, Asia
- ➔ Include studies of exposures to potentially important new causes of cancer (possibility of developing a priority plan).
  - Oil industry (Nigeria) with UNEP and STPH
  - Tattoos (German, France, and USA): 1 P1 scientist, 1 postdoctoral scientist
- ➔ To lead and support dissemination efforts in LMICs and help build up capacity in these countries.
  - Regional Codes Against Cancer: LAC, Asia next, Future: Africa and Middle East
- ➔ To prolong its policy to focus on areas where ENV can make a difference.
  - Locations, cancers, exposures that are understudied or challenging to study
  - Nigeria delta region and oil industry; Cancers – bladder (Malawi); Skin cancer in persons with albinism
  - Need for an impartial partner: Fukushima, radiation work, oil industry, Asbest cohort, future cohorts in the Russian Federation (coal mining)
  - A need for numbers: consortia leadership – childhood cancer (CLIC), AGRICOH/AGRICAN, AfrECC (Oesophageal cancer in Africa)
- ➔ To maintain critical mass in radiation research in Belarus, Ukraine, Kazakhstan, and Japan.
- ➔ To establish a position in exposure assessment, with a focus on LMICs-specific exposure circumstances.

S.W.O.T analysis: Environment and Lifestyle Epidemiology (ENV) Branch

Strengths

Multi-disciplinarity and diversity in expertise (epidemiology, biostatistics, oncology, environmental sciences, fieldwork methodology and public health) form a very strong and effective team

Open door policies at all hierarchy levels create a scientifically inspiring, respectful and friendly atmosphere which both contributes to the overall positive friendly atmosphere and promotes creativity, problem solving, collaboration and high-quality research in the Branch

Strong team spirit, trust and mutual support allow ENV to tackle scientifically and politically challenging projects, fulfilling the Agency's unique purpose

Excellent relationships and mutual support between supervisors and staff at all levels

A healthy mix of projects and programmes of work, including longer term and shorter term activities, those which are broad vs highly targeted, work based on secondary data and those on new fieldwork, allowing for flexibility and spreading of risks in terms of unexpected delays or other impacts on project performance (like the pandemic)

Success in launching projects in low-income countries and under-researched areas

Success in attracting extrabudgetary funding

Strong record of new fieldwork studies in LMICs, where research gaps are many

Extensive international network in occupation, radiation and environmental epidemiology and in cancer communication; extensive scientific networks across Europe, South America, Russia, Japan, Africa and North America

Collaborations with every single IARC Branch

Weaknesses

Smaller contribution from the IARC regular budget for staff positions than other Branches

ENV's research encompasses many topics with very few senior scientists, so the expertise depends on individuals and departure of staff requires replacement with same expertise to continue the work

Career development pathways are often less than smooth, which is a feature beyond ENV's control and inherent in the UN system structure for career development. The step from Early Career Scientist to junior Staff Scientist is relatively small in expertise but large in terms of overcoming system barriers

Promotions of P staff at the Agency are on hold for some years

Opportunities

With its broad expertise ENV can select research programmes that fit perfectly within the Agency's mission in cancer prevention research and "cancer research that matters"; the outcomes of ENV's research are highly relevant for cancer prevention

With its many consortia ENV provides Early Career Scientists ample opportunities to build a research network not only within IARC but also with external collaborators. These links are of great benefit when returning home and continuing a scientific career

Opportunities to specialize or gain experience in a broad range of topics, supported by strong methodological skills in the Branch. Further, ENV has a high degree of flexibility to initiate research on new topics and kick-start international collaborations efficiently

The contribution of the environment to the cancer burden remains to have numerous open research questions so there is no way that ENV will not remain "busy" for several upcoming decades

Although possibly seen as a weakness by some, the lack of strong expertise in molecular epidemiology and mechanistic research provides opportunities, as it allows partnering with the respective expertise in-house or with external partners, leading immediately to constructive partnerships as each one's territory is very clear

With its more recent and growing activities in cancer prevention projects, ENV has a key role in shaping the cancer prevention agenda

Threats

Dependency on success in extrabudgetary funding; this has worked very well for over 10 years but it is a possible threat with an unpredictable number of future calls for environmental and lifestyle epidemiology work

IARC budget constraints led to decrease in number and seniority levels of ENV regular budget staff positions, rather than increase as recommended in previous reviews from 2012 and 2017

Administrative workload of branch leadership and scientific staff has increased

International fieldwork requires hands-on presence on the ground, which has been disrupted during COVID, and even in normal times, takes up considerable amounts of time

Assessment of past performance and future plans

Past performance

ENV

Assessment of ENV's scientific quality: **Outstanding**

Assessment of the relevance of ENV's work to the mission of IARC: **Perfect fit**

Future plans

ENV

Assessment of ENV's scientific quality: **Outstanding**

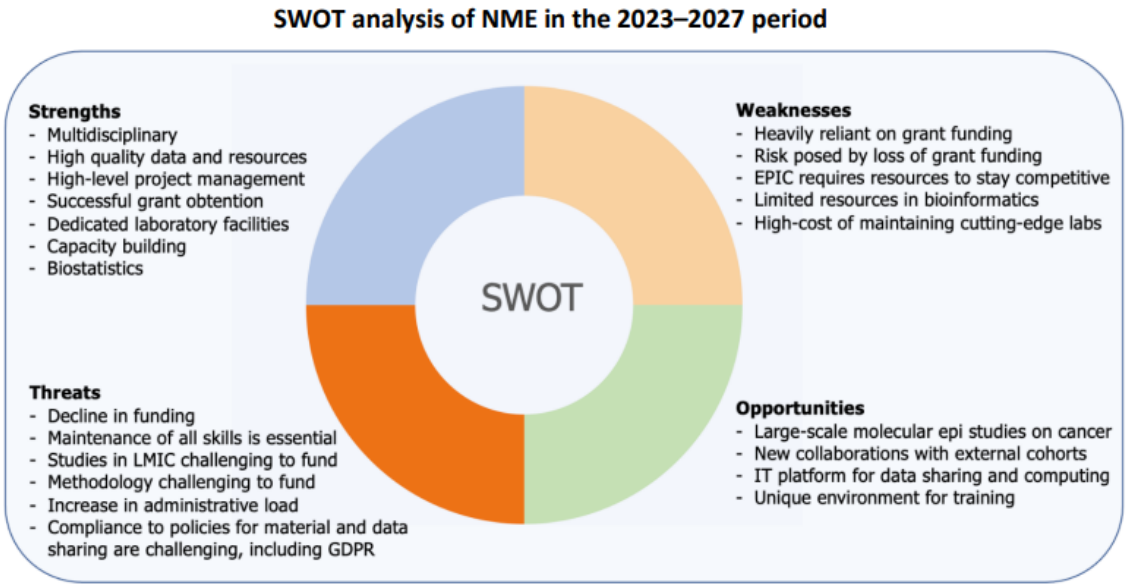
Assessment of the relevance of ENV's work to the mission of IARC: **Perfect fit**

Nutrition and Metabolism (NME) Branch Review (2023)

Recommendations from the Review Panel:

- Strongly supports NME's exceptional molecular and nutrition epidemiologic research integrating metabolomics, proteomics, hormone measurements and genomics within population studies.
- To evaluate the long-term sustainability of the in-house metabolomics platform (maintaining vs outsourcing).
- To maintain and upgrade the research infrastructure for EPIC data as well as sample replenishment for cancer cases where the biosamples have been depleted. Continued collection and centralization of repeated measures of diet and lifestyle factors during the long-term follow-up.
- To participate or initiate consortia for cancer survivors.
- To expand studies on multimorbidity by integrating additional existing resources and real-world databases.
- To carefully evaluate whether conducting lifestyle intervention trials is a high-priority research area for NME/IARC.
- To integrate the Precision Nutrition framework within NME's ongoing and future projects.
- To enhance efforts to conduct validation studies of novel dietary indices.
- To invest in new approaches for the pre-processing and statistical analysis of omics data for their use in cancer studies.
- To continue/strengthen research in LMICs and contribute to capacity-building in these countries.
- Support to EB-funded scientists (portion of RB support).

S.W.O.T analysis: Nutrition and Metabolism (NME) Branch



Assessment of past performance and future plans

Evidence Synthesis and Classification (ESC) Branch Review (2024)

Recommendations from the Review Panel:

- Recognize the unique aspects of each programme while continuing to foster synergies among resources, activities, and developments when appropriate.
- Integrate representatives from LMICs (IARC trainees, Visiting Scientists, Summer School attendees, observers, etc.) and early-career researchers into ESC activities to enhance global inclusion.
- Address concerns regarding short-term contracts for some staff members, exploring potential solutions to improve stability and retention.
- Maintain and expand efforts towards increased dissemination of ESC outputs. External advice on implementation and scientific communication could help broaden dissemination to policy-makers, stakeholders, the general public, and patient groups, particularly to combat disinformation.
- Recognize editing as a critical, labour-intensive step in evidence synthesis. Continue exploring ways to streamline and accelerate the editing process.
- Diversify external funding sources to strengthen the financial foundation of ESC programmes.
- Maintain ESC's rigorous efforts and strict policies to avoid conflicts of interest, ensuring the integrity and credibility of its outputs and evaluations.

S.W.O.T analysis: *IARC Monographs* Programme (IMO)

Strengths:

- Unique and strategic role in identifying the causes of human cancer, which is the first step in cancer prevention. In collaboration with cancer researchers at IARC and at leading institutions worldwide, IMO's Monographs and other publications provide a synthesis of available evidence on carcinogenic hazards of global relevance and contribute significantly to the science of carcinogenesis by pointing to critical gaps in knowledge related to human exposure, cancer epidemiology, cancer bioassays and mechanisms of carcinogens.
- Availability of expertise at IARC in the different areas of research used in Monographs evaluations. This expertise not only provides depth to the Secretariat during Monographs meetings but also facilitates strategic activity inside IARC involving other Branches in collaborative work with the Monographs scientists. IMO also advances methods for carcinogen evaluations and serves as an important catalyst for international collaborative research, including at IARC, on selected key agents and issues.
- Research integration efforts have resulted in many early-career scientists from other Branches of IARC joining the IARC scientific Secretariat at Monographs meetings; most of these scientists are from LMICs, which helps to broaden the coverage and interest of the Monographs topics and serves as a valuable training tool in the methods of systematic review.

We have successfully competed for an IARC-wide Visiting Scientist position from a LMIC who is conducting a systematic review on a high-priority topic in both LMICs and HICs.

- Worldwide recognition and use of the Monographs by national and international authorities and organizations to support actions to reduce exposure to carcinogens in the workplace, in the environment, and elsewhere.
- IMO's extensive network of external collaborators, built on organizing a large number of scientific meetings and workshops and through active involvement in training, capacity-building, and other scientific outreach activities globally. Activating this network within the past 5 years has allowed the recruitment of many Visiting Scientists and Senior Visiting Scientists to help cover expertise gaps in informatics, exposure science, epidemiology, cancer bioassays, and mechanisms of carcinogenesis. For example, two senior epidemiologists were recruited as Senior Visiting Scientists to help develop a scientific workshop and resulting IARC publication on bias assessment in observational cancer epidemiology.
- IMO's excellent senior leadership with, collectively, more than 20 years of Monographs' expertise, as well as a motivated and highly skilled scientific and technical staff, who collaboratively support the development of high-quality and timely evidence syntheses and carcinogenicity classifications with broad international impact.
- IMO's demonstrated success in recruiting top-calibre senior and junior scientific staff to fill recent gaps in key positions. IMO has taken advantage of recent retirements and departures to re-energize the exposure science, epidemiology, and toxicology scientific Secretariat. The eight Scientists hired or promoted during the past five years have brought new skills, knowledge, and motivation to carry out the important work of the Monographs. In particular, the hiring of new scientists in the area of mechanistic toxicology has refreshed the team's skills in this emerging discipline and has already resulted in important developments, such as a scientific workshop to further advance the use of the key characteristics of carcinogens, held in July 2023.
- IMO's exceptional degree of camaraderie in carrying out its mission. Over the past 5 years, Programme staff have taken collaborative training with the WHO Ombudsman's office in February 2019 and have undertaken strategic planning exercises, including an off-site retreat in September 2022.
- IMO's continued development and use of systematic review tools over the past five years. To help in maintaining and improving these important tools, IMO has successfully recruited a web developer, who has been improving the publication tools (IOPS, Table Builder, HAWC) and developing and deploying the "IARC Monographs Database Online" (IARC-MonDO), an enhanced database of the key information from Monographs evaluations. The web developer's skills in informatics will help optimize report outputs and infographics of the information in IARC-MonDO.
- IMO's substantially improved communication strategies. Some of the improvements realized over the past 5 years are scientific, such as the publication of its HAWC literature searches with each volume and the addition of detailed evidence synthesis sections in each monograph, to improve the transparency of its systematic reviews. Others are geared towards the wider community, such as the publication of questions and answers and infographics along with the scientific summary in The Lancet Oncology. IMO has launched a triannual newsletter to increase awareness of recent evaluations and to widely publicize the calls for data and experts for forthcoming meetings.

Weaknesses:

- The relatively small staff within IMO must coordinate the evaluation of highly heterogeneous agents, encompassing a range of complex scientific issues relevant to interpretation of data, particularly on cancer in humans and on mechanisms of carcinogenesis. This means that IMO must continue to rely on scientific resources outside of the programme and IARC. Furthermore, without additional funding, there will necessarily be many more agents suitable for carcinogenicity evaluation than can be carried out by the available staff.
- Advancing research needs that would inform Monographs evaluations, including launching research on agents prioritized by the Monographs is beyond IMO's mission. IMO cannot direct research resources to fill research gaps identified within the Monographs. However, IMO

scientists have been instrumental in initiating, facilitating, and contributing to research collaborations across IARC and major international institutions. Similarly, for maximal public health impact, Monographs evaluations need to be translated into action by other institutes and national authorities, which is also beyond IMO's control. IMO lacks resources to conduct extensive outreach to national and international organizations that could facilitate such translation.

- Under the IARC MTS, improving research translation to LMICs is a priority. Further work is needed to translate the relevance of IMO activities for LMICs to the wider WHO community, and to expand IMO's networks in LMICs.
- Over the past 5 years, there has been an increasing need for IMO and IARC Communications staff to address demands to better communicate hazard identification concepts to lay audiences. While demands for such communication are rising, the capacity to address the need could be improved either within IMO or by leveraging other IARC or external resources, if sufficient funding mechanisms were available.

Opportunities

- The work of IMO, which is a key strategic scientific programme of IARC, has garnered high international standing and scientific credibility. The 2018 Advisory Group to Recommend an Update to the Preamble continues to provide a roadmap to guide and strengthen the Monographs evaluations. Thus, a key opportunity is for IMO to further consolidate and enhance the current outstanding work on the Monographs, while expanding communication and dissemination methods to make this valuable information accessible and analysable, for example by the worldwide deployment of the IARC-MonDO database.

Threats

- **Preserve current core activity of IMO:** Inadequate ongoing funding may threaten the preservation of core Monographs activity, a risk heightened through lobbying from stakeholders and political pressure on major funding agencies. In addition, there is reputational risk to the Agency if conflicts of interest are inappropriately handled or if the high quality of Monographs evaluations is not maintained. Appropriate staffing and efficient organization across IMO will be required to produce three high-quality Monographs per year in a timely manner. In order to mitigate the risk of this funding threat, recent advances to improve collaboration within IARC and across WHO should continue, particularly with regard to planning, outcomes, and communication of Monographs with high relevance to other WHO programmes.
- **Maintaining high relevance of IMO's Monographs series:** The Monographs' Preamble was last revised in 2018. Over time, it will be necessary to revisit the Preamble to ensure that the methodology used in the Monographs is consistent with current state-of-the-art practice for systematic review and cancer hazard identification. IMO will continue its processes to optimize the methods used in its evaluations, by testing innovative methodologies at forthcoming meetings. Innovations that prove useful will be considered for formalization in future revisions of the Preamble (we envisage convening an Advisory Group to consider revisions to the Preamble within the next 5 years). As reliance on mechanistic and novel data streams increases, analyses of such data may help identify emerging or new priorities for evaluation. IMO has already benefited from feedback of its Working Groups after each meeting, in order to improve its process on a continuous basis. IMO sought input from key users when designing the IARC-MonDO database and would benefit from increased feedback from users of its products, including online assessment when accessing Monographs or online publications.
- **Timeliness and methods of updating the content:** The rapidly increasing pace of scientific publications in cancer research requires vigilance to ensure appropriate preparation or updating of published Monographs evaluations. There is a risk to the integrity of the programme if published evaluations are regarded as out-of-date. In particular, a focus on Monographs preparation practices should continue within IMO to improve quality, efficiency, cost-effectiveness, and timeliness. Furthermore, it will be critical for the Advisory Group to Recommend Priorities for the IARC Monographs during 2025–2029 to consider agents for re-evaluation on the basis of emerging evidence as well as first-time evaluations in providing guidance to IMO. Notably, the streamlined approaches recommended by the 2018 Advisory

Group to Recommend an Update to the Preamble to consider new cancer sites for agents already classified as Group 1 could result in improved estimates of cancer burden from occupational and environmental carcinogens but may require additional funding to permit a systematic evaluation of all 127 Group 1 agents to identify which new cancer sites may have sufficient or limited evidence for these agents and to convene Working Groups to review the evidence.

Impact of the evaluations and publications

- Measurement of the impact of Monographs evaluations is vital to demonstrate the need for the Monographs programme to users and funders. Additional case studies showing specific examples of change in public policies resulting from information generated by the Monographs programme would be valuable to IARC and other public health agencies. Associated published papers also provide objective parameters to judge the value of the programme over time, but they are insufficient as a comprehensive evaluation of impact.

S.W.O.T analysis: *IARC Handbooks* Programme (IHB)

Strengths:

The Programme:

- Fits perfectly in the WHO framework of the global noncommunicable disease (NCD) strategy.
- Has a unique and strategic role in assessing cancer-preventive agents, interventions and strategies: in collaboration with other Branches at IARC and cancer researchers worldwide, IHB provides critical reviews and consensus evaluations by international groups of independent experts of all publicly available evidence on the topic under review, through a transparent, rigorous and widely recognized process.
- Has benefited from the IMO methodologies in developing the Preambles.
- Has established strong collaborations with WHO headquarters and regional offices (WHO headquarters, WHO Regional Office for Europe, and WHO Regional Office for South-East Asia).
- Has provided the basis for the updated WHO Recommendations for screening and treatment of cervical precancerous lesions, with the evaluation of all cervical cancer screening strategies.
- Provides updated or first-time evaluations of numerous interventions and strategies that are of high priority for public health globally.
- Has developed strong synergy and efficiency through shared production resources within ESC (especially IMO) e.g. in the workflow, communication strategies, and systematic review tools.
- Draws on a pool of Working Group members from previous Handbooks and Monographs.
- Draws on the strong leadership of IARC research Branches in domains relevant to the Programme's activities.
- Receives worldwide recognition in providing evaluations that help planning for recommendations and cancer prevention strategies in individual countries.
- Is involved in collaborative work with other Branches/Teams, who benefit from IHB staff expertise.

Weaknesses:

- **Scope:** Topics such as health economics and cost-effectiveness are not addressed in the Handbooks Programme, although such approaches would be an added value to the product.
- **Expertise:** The Programme covers a wide range of topics for primary and secondary cancer prevention. This creates a challenge to the IHB scientific staff, who must show great flexibility and adaptability.
- **Staffing:** For each volume, topic-specific expertise is required for some subgroups (typically 3 or 4 subgroups in total); the programme relies on appointments of ECVS (postdoctoral scientists, Visiting Scientists, and Senior Visiting Scientists) with topic-specific expertise. This process is time-consuming, to find and recruit the relevant candidates and to train them for the work at hand.

- **Dissemination:** Dissemination of the scientific content of the Handbooks could be improved. The information is not easily accessible to a public not familiar with the website. Communication and dissemination through other channels must be developed.
- **LMICs:** Evaluation of prevention strategies for low-resource settings is becoming increasingly important because the challenges in implementing prevention strategies in these settings are different compared with those in high-income countries. However, current evaluations are primarily based on evidence coming from high-income countries. This must be taken into account when making evaluations that also apply to these settings.

Opportunities:

- **The scope of the programme:** The new Preambles provide a transparent and rigorous framework for evaluations of primary and secondary prevention interventions in a more systematic manner. The 2-volume series on Alcohol Control fits perfectly with the scope of the Programme under these Preambles.
- **Establishing collaborative networks with other IARC Branches, WHO, and other national or international institutions**: The co-location of the three programmes on the same floor of the new IARC building will give more opportunities for cross-disciplinary collaborations within the ESC Branch.
    - IHB has also interacted with the other IARC Branches for past meetings. For the upcoming meetings (Volumes 21 and 22), IHB will establish a collaboration with the Lung Cancer Working Group and the Gastric Cancer Prevention Team, respectively.
    - IHB is strengthening its link with WHO, with both headquarters and regional offices. Notably, Volume 20B will be prepared in close collaboration with the WHO Regional Office for Europe, and Volume 21 will be in close collaboration with WHO headquarters.
    - IHB is currently involved in a project with the World Cancer Research Fund (WCRF) (see Section 1.2.1). Collaboration with WCRF may be envisaged for Handbooks on primary prevention related to diet, nutrition, body weight, and physical activity.
    - The Centers for Disease Control and Prevention (CDC) is funding the Programme for 5 years (2023–2027). In case a topic planned for review would be of particular interest to them, IHB may consider also scientific collaboration with the CDC.
- **Workflow:** We have adapted our workflow to the new developments (scoping meeting, 2-part meeting with subgroup remotely and plenary on-site), which will be systematically integrated in the preparation of each volume.
    - The "Coordination and communication mechanisms between IARC and WHO – at management and working level" document that is tailored for the Handbooks Programme is currently under development with WHO.
- **Data management tools:** IHB implements or adapts, as much as possible, the technologies developed for the preparation of the Monographs, depending on relevance and other factors, and seeks alternative processes if needed.
    - The IARC Online Publications System (IOPS), which facilitates document management and exchange with the Working Group members, is currently undergoing a thorough and comprehensive review and update of its codes and functions, led by the web developer (M Rose) who is shared between IHB and IMO.
    - Development of editable templates in Table Builder (developed and maintained by the Monographs Programme) that can be easily adapted specifically for each volume;
    - Use of HAWC (coordinated and maintained by the Monographs Programme) for better transparency of the literature selection process.

Threats:

- **Frequency of volumes:** The funding and staffing secured during the past 5 years are adequate for a schedule of one meeting every 15–18 months. Production of one volume per year, as originally planned in 2014, would require additional fixed-term scientific staff, from the Regular Budget, as well as additional General Service support staff.
- **Timeliness of publication** is essential to the credibility of the programme. Publication within a reasonable time after the meeting is currently not achieved. Although scientific staff has

increased and Volume 20A is scheduled for publication 12 months after the meeting, the bottleneck has become the editing step. IHB requires a dedicated editor for a more expeditious publication.

- **Translation of the results into recommendations:** Evidence-based evaluations must be translated into recommendations to be useful to improve public health. Despite the high recognition of the value of the IARC Handbooks by the scientific community, the programme must enhance its visibility and increase access to policy-makers, to facilitate translation of the evaluations into recommendations.

S.W.O.T analysis: WHO Classification of Tumours Programme (WCT)

Strengths:

- Well-established WHO and IARC flagship programme with a track record of extreme success with considerable international impact.
- The tumour classification produced is mainly research evidence-based and not eminence-based and provides a multidimensional viewpoint of tumours.
- Classification of tumours is a necessity for patient diagnosis, management, prognosis, and prediction as well as all forms of cancer research, from etiology to treatment.
- The WHO Classification of Tumours series is a major resource for pathologists, epidemiologists, cancer registries, cancer researchers, oncologists, molecular pathologists, geneticists, and others involved in cancer detection and prevention.
- Clear strategy for the 5th edition (including move to process and risk management, SOPs, evidence review, and layout in-house) and moving on to the 6th edition on a strong base.
- Standing and expert editorial board system working very well; tremendous support from the pathology community and other disciplines.
- The 5th edition had a managed process with structured sections for each tumour type.
- Small but dedicated in-house WCT team committed to all WCT projects, not only the WHO Blue Books.
- The production process of the books has been streamlined with defined workflows.
- IT expertise is available within the programme with in-house development of BBOSS allowing online submission of content and BBEST allowing editor/author identification based on bibliometrics.
- The WHO Classification of Tumours Online website has been implemented, enabling individual and institutional subscriptions with discounts for LMIC settings and trainees.
- Therefore, WCT is not dependent on a single source of funding. Sales figures for WHO Blue Books and for the website remain excellent.
- With implementation of the website there is increased community participation, and an image library including whole slide images is being built up.
- New collaborations have been established (IC^{3}R) to collate research findings and translation to clinical practice through WCT, and projects (WCT EVI MAP and EVI PAT) have been implemented to strengthen the evidence base and to promote evidence-based pathology provision for WCT and training, respectively.
- Cytology reporting systems have been implemented, strengthening cancer diagnosis and research especially in LMIC settings.
- WCT provides histology services and pathology expertise for research to multiple groups within IARC, and provides senior pathology expertise and advice within WHO.
- Strong international collaborations have been established.

Weaknesses:

- The speed with which the books are produced after completion of writing is limited due to staff constraints (especially copy editing). Book production of the last six volumes of the 5th edition is pending; however, beta versions are available on the website.

- The same tumour occurring across different organ systems requires improved harmonization across volumes.
- The research evidence available and included is of varying quality.
- The negative impact of molecular-only classifications in countries or regions without molecular backup is a concern.
- WCT's status as a programme reduces the externally perceived importance of pathology as a discipline within IARC and WHO, when it is in fact the basis of cancer research, despite the potential managerial advantages of having the three publication programmes in one Branch.
- IARC and WHO do not control all the content required for the WHO Blue Books, which are more than just pathology (e.g. staging of tumours, UICC staging).
- WCT does not control the distribution of the print version of the WHO Blue Books, which is in the hands of WHO Press, who have limited space for storage. They also handle relationships with booksellers, including discounting and shipment.

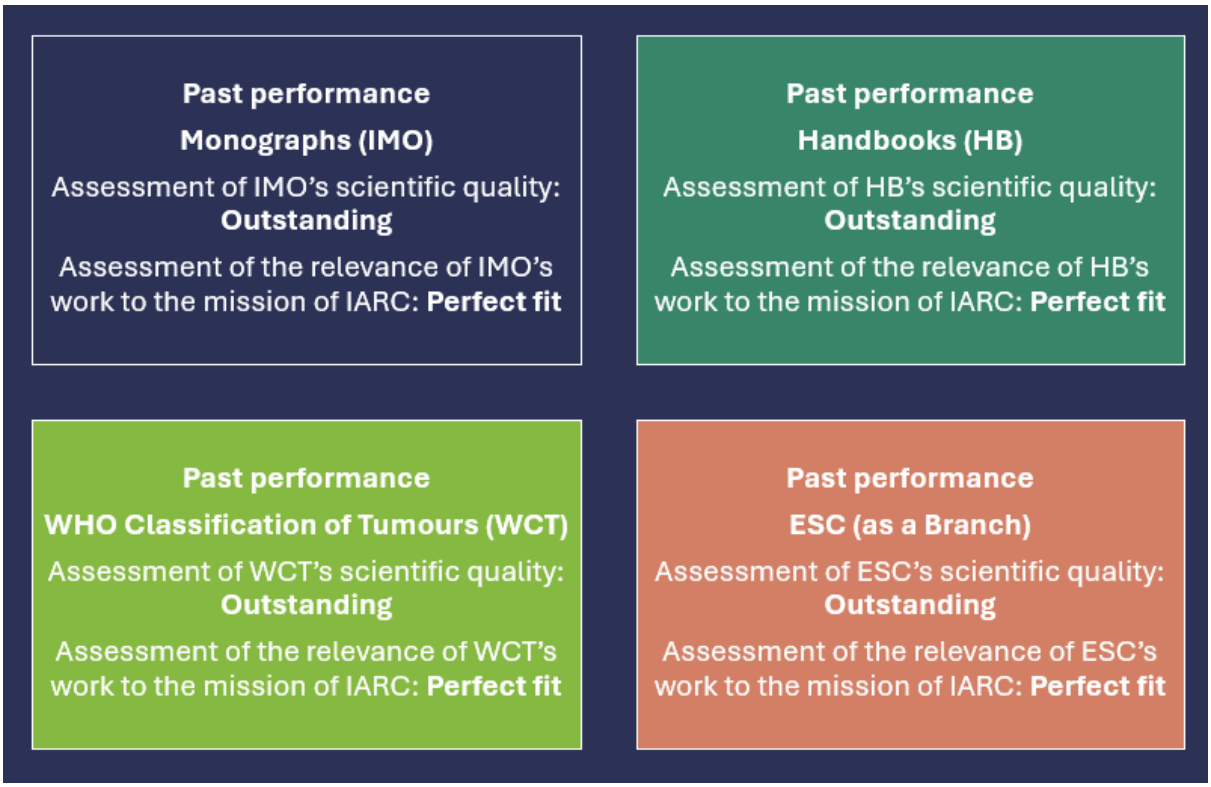
Opportunities:

- The start of the 6th edition gives us the opportunity to continue those methods in the 5th edition that worked well, as well as to review and update the 5th edition content based on new evidence without rewriting.
- Opportunity to address the weaknesses identified in the WHO Classification of Tumours programme and to rectify them or to minimize their impact for the 6th edition.
- Implementation of the website will eventually replace print books in the future, reducing the cost incurred in book production.
- Building a web-based whole slide image library will promote digital pathology to allow the development of AI tools facilitating comparison with patient tumour images by end-user pathologists.
- The IC^{3}R collaboration will facilitate the generation of research while maintaining quality, and the translation of research into practice, and encourage accreditation of research laboratories similar to clinical laboratories, to ensure the quality of evidence generated.
- The WCT EVI MAP project will allow the generation of maps of research evidence gaps, promoting new research, develop hierarchical levels of evidence pertaining to pathology, and develop tools of measure to evaluate its quality, thereby improving the quality of cancer research in general and particularly those cited in future WHO Classification of Tumours volumes.
- The website will allow the display of evidence levels quoted in the WHO Classification of Tumours and evidence gap maps, with live updates based on new research evidence as it emerges.
- Standardizing cytology reporting by the introduction of cytology reporting systems will promote its use in research, allowing more accurate category-based risk of malignancy assessment for atypical and suspicious for malignancy categories.
- The pathology services and support for research within the Agency are enhanced through the well-equipped histopathology laboratory and the senior-level pathologists available with WCT.
- There are research opportunities related to the classification of tumours in several areas, particularly in evidence assessment (systematic review), computational pathology, and molecular pathology, which fit well with WCT's role within IARC.
- Opportunities are available to provide international leadership in the practice and development of pathology, primarily through coordination between the organizations within the discipline, especially to reduce the impact of molecular-only classifications in countries without molecular backup. This may include a WHO framework for pathology support in LMIC settings.
- There are opportunities to attend pathology and other cancer conferences to highlight the WHO Classification of Tumours, to increase the use of the WHO Blue Books beyond the pathology community, and to enhance the visibility of WHO and IARC, with the aim of attracting more participating states for IARC.

Threats:

- WCT Staff: we have a small team with a big job. Movement of staff due to mandatory retirement and better opportunities and replacing those with temporary appointments impacts our capacity, leads to publication delays, and continues to be a threat to our future work. Also, as new WCT projects get off the ground the small number of WCT staff is stretched to its maximum.
- Information science and technology are a particular concern; we need more staff and the infrastructure to support this.
- Printing costs of books are high, and income depends on sales, so value for money is a potential concern. More than 90% of the books are bought by pathologists, and web subscriptions are often made from personal funds. However, most do understand the expensive nature of publishing and accept the current model as the best option available.
- Other organizations could try to produce their own classifications if WHO is seen to regard the WCT programme as being less important.
- The impact of molecular-only classifications in countries or regions without molecular backup may alienate these pathologists from the WHO Classification of Tumours.

Assessment of past performance and future plans



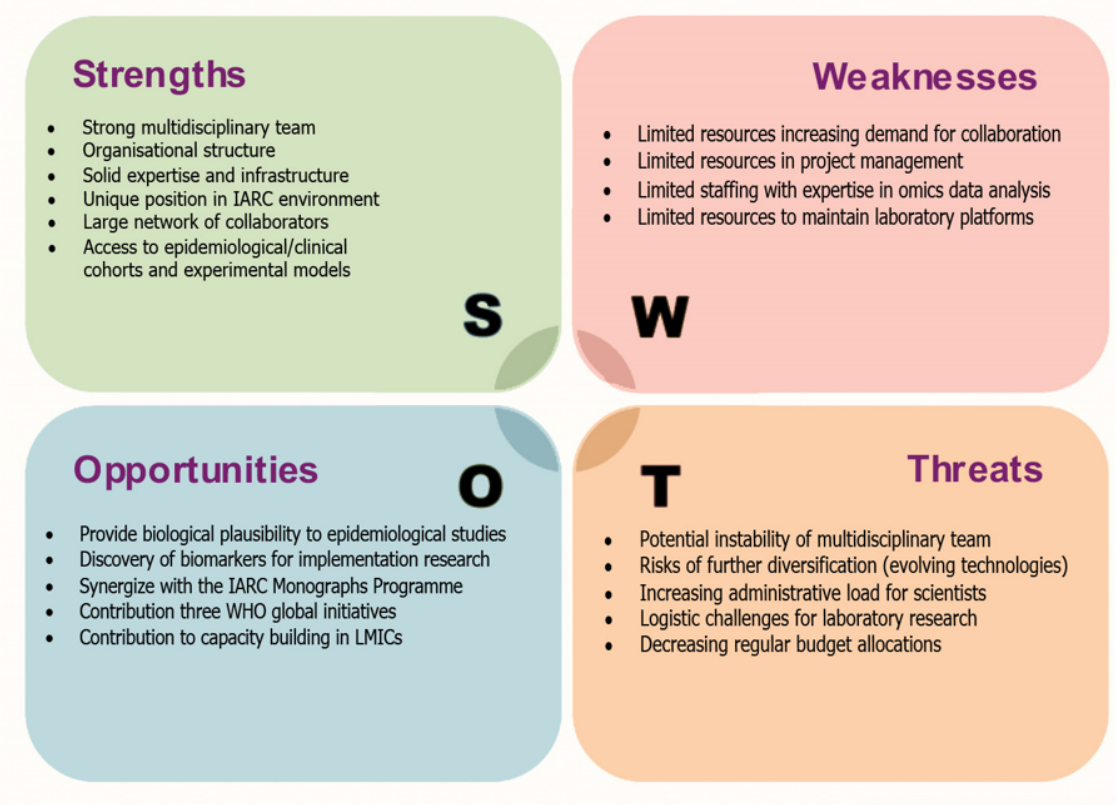
2025 Branch Reviews

Epigenomics and Mechanisms (EGM) Branche Review (2025)

Recommendations from the Review Panel:

- ➔ Preserve EGM's interdisciplinary role and if restructuring occurs, maintaining EGM as a cohesive unit within another Branch would best preserve its methodological expertise.
- ➔ EGM's access to global population cohorts, particularly in LMICs, and expertise in mechanistic research focused on the epigenome should be sustained. Its training programs for junior scientists from LMICs, who later become international collaborators, are also valuable assets.

- Expanding translational research is commendable but should prioritize areas with immediate public health impact.
- EGM must prioritize research based on mission alignment rather than EGM survival, ensuring focus on areas with the highest impact while optimizing resource allocation.
- Improve communication and visibility. The Review Panel observed that while EGM presents a large volume of work, identifying specific areas of excellence is challenging.
- Scientists and staff should receive strong mentoring, clearer support for career development, and increased opportunities for inclusion within IARC's broader institutional framework.



SWOT analysis: Epigenomics and Mechanisms (EGM) Branch

Early Detection, Prevention and Infections (EPR) Branch Review (2025)

Recommendations from the Review Panel:

Scientific Portfolio

- Regular branch planning activities should be implemented to achieve greater strategic alignment, balance, and prioritization across EPR's research portfolio.
- Strengthen integration of infection-related cancer prevention to maximize impact.
- Continued investment in building research capacity within LMICs will strengthen global cancer prevention efforts.
- Expanding EPR's implementation research portfolio is encouraged, with engagement of external expertise in behavioral science and health economics to enhance effectiveness.
- A strategic framework should be developed to incorporate emerging technologies such as artificial intelligence, large language models, and multicancer early detection in EPR research.
- Greater integration of patient and community perspectives across all research stages will improve relevance and impact.

- ➔ Sustain support for WHO cancer initiatives: IARC's essential contributions to WHO's global cancer initiatives should continue to be strengthened.
- ➔ Expand and secure funding for CanScreen5 expansion.

Management and operations

- ➔ Increase core budget support for EPR.
- ➔ Systemic challenges limiting equitable career progression for scientific and non-scientific staff should be addressed to enhance retention and professional growth.
- ➔ Reduce administrative burden to allow scientific staff to focus on research activities.
- ➔ Improve support for Early Career and Visiting Scientists (ECVS), including assistance with relocation, housing, and other challenges.
- ➔ Strengthen team cohesion through regular team-building.
- ➔ Structural solutions should be explored to enable appropriate engagement with the private sector while maintaining IARC's scientific integrity.

SWOT analysis: Early Detection, Prevention, and Infections (EPR) Branch

Strengths:

- EPR has established a reputation in generating authentic and credible scientific evidence to guide policies in cancer control. This has reinforced IARC's brand value as a trusted organization conducting high-impact research with integrity.
- The new organizational structure of the Branch has helped scientists to foster collaboration and identify synergies within the Branch.
- EPR has highly motivated and high-performing personnel with a broad range of skills and expertise. In 2021–2023, EPR generated an average grant funding amounting to €571 799 per P-staff (the highest among all IARC Branches).
- Renewed, strong, and stable leadership with reorganization of the Branch. The Branch Head and Deputy Branch Heads are on Regular Budget and have at least 5 years of service at IARC.
- EPR has a broad remit of geographically diverse projects for optimal public health impact, with a strong focus on LMICs.
- EPR's research directly contributes to national and international policies and guidelines due to the selection of contemporary and relevant research topics and regular interactions with national and international organizations.
- Some of the EPR's research outcomes have had significant public health impacts (e.g. cohort study on single-dose HPV vaccination; randomized controlled trials on clinical breast examination and thermal ablation; randomized controlled trials and observational studies on *Helicobacter pylori* and gastric cancer).
- The programme on infection-attributable cancer burden is a key global reference.
- Cutting-edge modelling to support public health decision-making, in both methods development and application, has added a new dimension to EPR's research.
- Strong focus on implementation science with multiple funded projects. Some of these are addressing vulnerable populations in both LMIC and HIC settings.
- Ability to attract significant funding from diverse sources (NCI/NIH, European Commission, Gates Foundation, CRUK, UK MRC, Gulf CDC, IDB, Sabin Vaccine Institute, etc.). The EPR grant amount in 2021–2023 (€22.9 million) was the highest in the Agency.
- High-impact Open Science publications to disseminate findings and support decision-making. The number of publications between January 2021 and April 2024 was 229 (h-index: 24).
- Scientists either are leading or are involved in key Agency Research Teams.
- EPR significantly invests in capacity-building and web-based training resources to improve public health and strengthen public health systems in cancer prevention and early detection.
- Extensive and committed collaborative scientific networks across the globe.
- Effective collaboration with WHO, the UN, and national governments to influence global and national policies.

- Cross-Branch collaborations.

Weaknesses:

- Limited number of staff (the majority being ECVSs), overcommitment due to demand from Participating States, and heavy workload.
- Heavy dependence on external funding, and constant effort is required to apply for new funding.
- Opportunities for further scientific collaboration with LMICs are restricted due to limited funding.
- Limited research expertise in-house in qualitative research methodology, policy impact, behavioural science, and health economics.
- GDPR regulations impacting data transfers within Europe.
- Lack of long-term funding options to guarantee full lifespan (>10 years) of research programmes (e.g. the CHRONOS and CanScreen5 projects should be ongoing projects).
- Difficulties in hiring and retaining staff from outside of the EU, especially those from LMICs.
- Too many staff positions on extramural budget have a negative impact on research activities due to lack of staff continuity.
- Reduction in senior P-staff positions funded through Regular Budget over the past few years.
- Communication of the value and impact of the EPR research needs to be strengthened.
- IARC is often seen as a funding agency instead of a research agency alone by the Participating States.

Opportunities:

- The large network of collaborators from diverse settings can be harnessed to plan new projects and apply for funding.
- Funding allocated from the Regular Budget every biennium and significant savings from extramural grants allow EPR to seed new projects and/or conduct hypothesis-generating studies in LMICs.
- The WHO global initiatives as well as a strong focus on improving cancer control within the countries have created a huge demand to conduct research in cancer prevention, cancer early detection, and implementation science.
- The new IARC Participating States see value in EPR initiatives in generating evidence, supporting implementation, and developing trained human resources in cancer control.
- EPR/IARC is well recognized by the European Commission to support implementation of the Europe's Beating Cancer Plan (some of the direct fundings to EPR/IARC are included in the plan).
- There is a global demand for cancer prevention knowledge and guidelines; existing collaboration between EPR and the WHO Academy can be leveraged in multiple areas.
- EPR can take advantage of expectations from Participating States and an increasing demand for country-level support. Recent administrative changes at IARC/WHO haves created better opportunities for engagement with the private sector and non-state actors, while ensuring independence and freedom from conflict of interest though compliance with the WHO Framework of Engagement with Non-State Actors (FENSA).

Threats:

- Obtaining new research funding opportunities is becoming more difficult continually, especially with the national funding increasingly being more restrictive. Reduction in funding opportunities worldwide due to the global financial crisis and low prioritization of cancer research.
- Ineligibility of IARC to compete for certain research grant calls for being an international organization and/or for being an organization based in a high-income country.
- The implementation of research studies may be delayed or the participation in the research projects may be restricted due to the increasingly stringent regulations in data and sample sharing and clinical research.

- Inability to attract scientists/clinicians for the professional positions from diverse settings due to the restrictive service conditions and lack of job security.
- Non-renewal of RB funded scientific posts and support staff.
- Limited opportunities for career development for junior researchers within IARC.
- IARC, as an international organization, is well placed to weather political change. Nevertheless, long-term impact assessment projects in LMICs remain susceptible to national/local political unrest, changes in health policy, and/or mobility of key collaborators.
- Risk of losing support from the collaborators, Participating States, and national governments due to changing political climate and increasing competition, etc.

Assessment of the Research Teams

Concept of Research Teams

The concept of IARC Research Teams was developed to facilitate the scientific work within and across IARC's research Branches by reducing the silo approach within Branches and introducing a more flexible modality of scientific collaboration on closely related research, in order to better implement the MTS 2021–2025.

Teams are informal organizational units within a research Branch or across Branches. The main task of a Team is to manage the implementation of two or more thematically related research or technical projects towards a common goal. The creation of Teams is based on needs and added value.

For the period of the MTS 2021–2025, the Research Teams are organized according to the following 7 categories: WHO Global Initiatives, Cancer-Focused, Functional Cancer Genomics, Metabolism, Methodological Innovations, Cancer in Informative Populations, and Cancer, Public Health, and Society. In 2024, there are currently 20 Research Teams, as listed below.

- **IARC Teams related to WHO Global Initiatives**
  - IARC Global Breast Cancer Initiative (GBCI) Team
  - IARC Cervical Cancer Elimination Initiative (CCEI) Team
  - IARC Global Initiative for Childhood Cancer (GICC) Team
- **Cancer-Focused Teams**
  - Oesophageal Cancer Team (ECA)
  - Gastric Cancer Prevention Team (GCP)
  - Oral Cancer Team (OCT)
- **Functional Cancer Genomics Team**
  - Rare Cancers Genomics Team (RCG)
- **Metabolism Teams**
  - Onco-Metabolomics Team (OMB)
  - Metabolic Epidemiology Team (MET)
  - Hormones and Metabolism Team (HorM)
- **Methodological Innovations Teams**
  - Risk Assessment and Early Detection Team (RED)
  - Population-Based Long-Term Surveillance Team (LTS)
  - Biostatistics and Data Integration Team (BDI)
  - Lifestyle Exposure and Interventions Team (LEI)
- **Cancer in Informative Populations Teams**
  - Nutrition, Cancer, and Multimorbidity Team (NCM)
  - Occupational Cancer Epidemiology Team (OCE)
- **Cancer, Public Health, and Society Teams**
  - Cancer Inequalities Team (CIN)
  - Health Economics and Cancer Team (HEC)
  - Public Health Decision Science Team (PHDS)
  - Research for Implementation Team (RFI)

In addition to the IARC Research Teams, a Communications and Dissemination Team (CDT) has been created.

Terms of reference and assessment of Research Teams

The terms of reference of the IARC Research Teams rely on the following criteria:

- A **set (cluster) of interconnected scientific/technical projects** with closely linked goals,
- **Alignment of overall Team goal with IARC's vision, mission, and priorities**, as spelled out in the relevant Medium-Term Strategy 2021–2025,
- Provision of:
  - **a rationale for the Team**, including: the added value of the proposed Team, the coherence of projects to be managed by the Team, and the envisioned and measurable impact of the Team's work,
  - a clear, relevant, and distinct **overall goal**,
  - **a 2-year workplan**, including milestones and specific deliverables,
  - a **resource mobilization plan**, including grant opportunities,
- **Collaboration across Branches**.

The benefits of implementing IARC Research Teams have been assessed during 2024, based on the Terms of Reference as well as the specific indicators listed below:

- **Governance:** governance and coordination meetings, collaboration with WHO
- **Collaborations:** cooperations across IARC Branches, collaboration with external partners
- **Workplan progress:** projects and consortia, applications and grants, publications, training
- **Main innovation and contribution to the MTS implementation**
- **Next steps and main challenges**

As part of the MTS evaluation, 17 Research Teams were assessed in 2024. Two Research Teams – the Health Economics and Cancer Team (HEC) and the Metabolic Epidemiology Team (MET) – were not assessed because they are not active following the departures of their Team leaders in 2021 and in 2024, respectively. The Research for Implementation Team (RFI) was not part of the assessment because it was created recently (in February 2024). The Communications and Dissemination Team (CDT) was not assessed because it was implemented recently (in 2023).

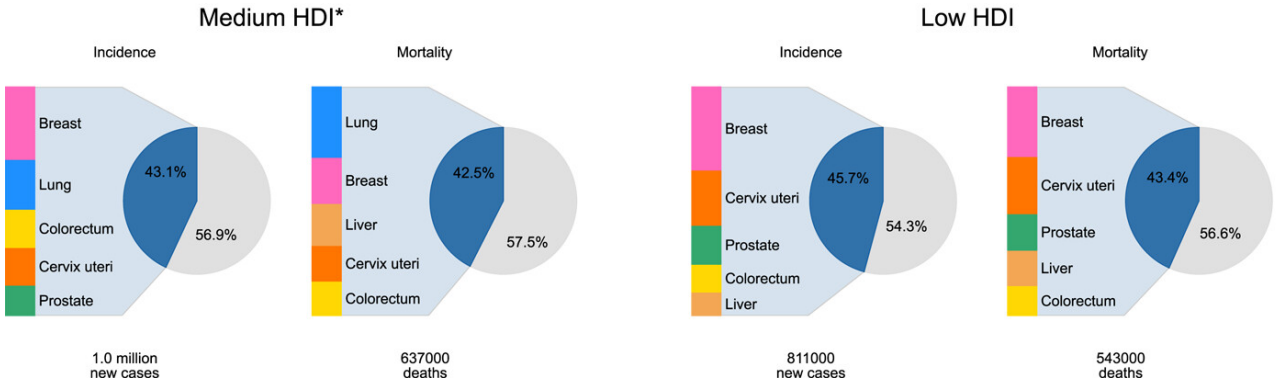
The main conclusions and recommendations of the Research Teams assessment are presented below. The individual assessments of the Research Teams are detailed in the next part of the document, according to the 7 categories of Teams.

Conclusions of the assessment of Research Teams

1. The assessment of the Research Teams demonstrates the **overall benefits of the Teams for the coordination of IARC's scientific programmes** and their significant contributions to the **implementation of the MTS 2021–2025**. The Research Teams directly contribute to:
   - Provide better visibility, knowledge, and communication about the IARC scientific projects across the Agency, relying on a bottom-up approach of research focus,
   - Reinforce cooperation across IARC Branches, reducing silos within IARC and contributing to the value chain of cancer research,
   - Target and reinforce collaborations with external scientific partners,
   - Consolidate information sharing and coordination with WHO headquarters through a more structured approach, especially on the WHO global cancer initiatives,
   - Better coordinate the selection and the preparation of grant applications, with various contributions across the Agency,
   - Explore some innovative scientific concepts and prepare the future scientific programmes of IARC,
   - Allow early-career scientists to coordinate the implementation of projects within a Team.

2. The assessment of the Research Teams also reveals **some limitations to this model** that was experimented with during the MTS 2021–2025, which will need to be addressed for the preparation of the next MTS, especially:
- The Research Teams model is characterized by some heterogeneity in terms of organization, ambitions, funding, and scientific outcomes,
- Some Teams are mainly intra-Branch (corresponding to the former "Groups" of the IARC organization for the MTS 2016–2020) and do not really contribute to synergies among scientific Branches,
- The involvement of Team members and especially the investment of Team leaders is not officially recognized as part of IARC's annual performance review (PMDS) and career development,
- Because the Research Teams were built on an informal model with no administrative component, some Team leaders mentioned the lack of dedicated resources for Team coordination.

3. The assessment of the Research Teams points to the necessity to simplify and **merge the 7 Teams categories, in order to focus on 2 priorities**: Cancer-Focused Teams including WHO Global Initiatives, and Methodological Innovations Teams, such as RED and PHDS.
   - ➔ In that context, IARC should consider merging certain Research Teams that address similar topics. For example, combining the Hormones and Metabolism Team with the IARC Global Breast Cancer Initiative Team could enhance IARC's efforts to address breast cancer more effectively.
4. The assessment of the **Cancer-Focused Teams** demonstrates that this model **is extremely relevant**, with highly successful Research Teams such as CCEI and GCP. In addition, it is worth recalling that [29% of global funding for cancer research is allocated according to specific cancer sites].
   - ➔ IARC should also guarantee the coherence of the Cancer-Focused Teams with its mission of cancer research and prevention, with a specific investment in LMICs. The data from GLOBOCAN 2022 indicate that the **cancers** with the highest incidence and mortality **in LMICs** are **breast, lung, colorectal, prostate, liver, and cervical cancer**.



Cancer Incidence and mortality in LMICs, Globocan 2022[27]

IARC has already established Cancer-Focused Teams on cervical cancer (CCEI), childhood cancer (GICC/WIT2C), breast cancer (GBCI), gastric cancer (GCP), oral cancer (OCT), and oesophageal cancer (ECA). Considering the GLOBOCAN 2022 statistics on cancer incidence and mortality in LMICs, IARC should also encourage Research Teams on lung cancer, colorectal cancer (including early-onset colorectal cancer), liver cancer, and prostate cancer. Some existing Research Teams are well positioned to cover some of these cancer sites, such as RED and RCG for lung cancer and OMB and LTS for colorectal cancer.

The assessments for each Research Team are detailed in the following pages.

[27] Source: https://doi.org/10.3322/caac.21834

1

Assessment : Cancer types Teams

Childhood Cancer Awareness and Research Evidence (CCARE) Team

Cancer types Teams
➔ Starting date: March 2023

Members

Team leaders: Dr Eva Steliarova-Foucher, Cancer Surveillance Branch (Scientist, CSU) and Dr Akram Ghantous, Epigenomics and Mechanisms Branch (Scientist, EGM) - Secretary: Dr Neimar de Paula Silva (Postdoctoral Scientist, CSU)

Team members: The Team comprises 21 team members from 6 Branches (CSU, NME, ENV, EGM, EPR and ESC, with support from the Director's Office.

➔ Dr Véronique Chajès (DIR); Mr Clément Chauvet (DIR); Senior advisors: Dr Freddie Bray (Branch Head, CSU), Dr Joachim Schüz (Branch Head, ENV), Dr Zdenko Herceg (Branch Head, EGM) and Dr Mary Schubauer-Berigan, (Branch Head, ESC). Members: Dr Ceren Süngüc (Postdoctoral Scientist, CSU); Dr Inge Huybrechts (Scientist, NME); Dr Shiny Manohar (IARC Postdoctoral Fellow, NME); Dr Zisis Kozlakidis (Scientist, Laboratory Support, Biobanking and Services [LSB]/NME); Dr Andre Carvalho (Scientist, EPR); Dr Ann Olsson (Scientist, ENV); Dr Ljubica Zupunski (Scientist, ENV); Dr Michele Matta (Scientist, ENV); Dr Rita Khoueiry (Scientist, EGM); Dr Farah Nassar (Postdoctoral Scientist, EGM); Dr Elisa Pasqual (ESC); Ms Véronique Terrasse (COM).

Objectives

Context

Each year, nearly 400 000 children aged 0–19 years develop cancer, and about 90% of these cases occur in LMICs. Whereas children in high-income countries have a more than 80% chance of surviving cancer with optimal care, survival rates for those in LMICs tragically range from only 15% to 45%. In response to this critical situation, WHO launched the Global Initiative for Childhood Cancer (GICC) in September 2018, in collaboration with St. Jude Children's Research Hospital in the USA. The GICC aims to achieve a global survival rate of at least 60% for children with cancer while ensuring reduced suffering for every child. Using the "CureAll" framework, the GICC coordinates stakeholders across sectors toward a common objective.

The GICC has two key objectives:

1. Capacity building: To enhance the ability of countries to provide high-quality information and services for children with cancer.
2. Prioritization of childhood cancer: To elevate the importance of childhood cancer on global and national agendas.

Launched in March 2023, the WHO-IARC Team on childhood cancer aims to improve information sharing and dialogue between IARC and the GICC team at WHO headquarters. The CCARE Team's ambition is to leverage ongoing research at IARC, foster coherent collaboration with WHO headquarters in support of the GICC, translate research findings into actionable strategies, and identify synergistic areas of work.

To achieve these objectives, the team members engage in regular meetings, both internally within IARC and with WHO partners. The specific goals of the CCARE Team include:

- Enhancing internal communication and identifying synergies in childhood cancer research.
- Streamlining the dissemination of knowledge generated by IARC on childhood cancer.
- Supporting the WHO GICC by providing scientific evidence to inform global actions.

Goal	By 2030, achieve at least 60% survival for childhood cancer globally and reduce suffering for all **Save one million additional lives**
Objectives	1. Increase capacity of countries to provide quality services for children with cancer, and 2. Increase prioritization of childhood cancer at the global, regional and national levels **Implemented across 6–10 countries (by 2019–2020) and 18–25 countries (by 2021–2023)**

Outputs & activities	National	Regional	Global
	Country assessment, case studies, support and implementation plans	Regional assessment and dialogues, snapshots and policy briefs	Global framework, technical package, dashboard and advocacy materials

Workplan progress

Projects and consortia

The CCARE Team is engaged in several key projects aimed at enhancing knowledge and improving outcomes for childhood cancer globally. Key initiatives include:

- **International Incidence of Childhood Cancer (IICC):** This project processes and disseminates data from population-based cancer registries worldwide, creating a unique resource on childhood cancer incidence. The latest volume (IICC-3) was supported by the Union for International Cancer Control (UICC).
- **International Classification of Childhood Cancer (ICCC):** A standardized system categorizing paediatric cancer types according to WHO guidelines, facilitating consistent reporting of childhood cancer statistics globally.
- **Childhood Cancer Registration Development (ChildGICR):** This initiative focuses on enhancing childhood cancer registration in LMICs through educational programmes and implementation research, in collaboration with St. Jude Children's Research Hospital.
- **Cancer Risk in Childhood Cancer Survivors (CRICCS):** Using quality-assured data from cancer registries, this project aims to estimate the number of childhood cancer survivors, assess their risk of second cancers, and develop guidelines for studying survivorship.
- **Childhood Cancer and Leukaemia International Consortium (CLIC):** A collaborative effort among more than 20 studies investigating the etiology of childhood cancer, particularly environmental causes, with a focus on leukaemia. CLIC is expanding its scope to include childhood brain tumours.
- **Childhood Cancer – Epidemiology, Research, and Omics (CICERO**): This multidisciplinary project investigates childhood cancer in Africa, focusing on ascertainment completeness, referral patterns, survival, and treatment completion, while also defining molecular profiles of cases.
- **CIRE-RF Study:** A registry-based case-control study examining the association between childhood cancer and exposure to radiofrequency electromagnetic fields.
- **Childhood Leukaemia and Environmental Risk Factors (CLERF):** A pilot study in Germany investigating the feasibility of recruiting patients with leukaemia for etiological research on gene-environment interactions.

Governance

Meetings:

- The preparatory meeting for the CCARE Team was held on 25 January 2023.
- Since its formation, the Team has convened four meetings during 2023-2024, adopting the name CCARE in July 2024.
- The Team meets on average once a quarter.
- In addition to these regular meetings, smaller technical meetings are frequently held for organizational and communication purposes among the co-leaders.
- Minutes of the meetings and all relevant documents are stored in the Team channel for easy access.

Collaboration with WHO

- The CCARE Team has established a close partnership with WHO headquarters to ensure effective coordination for the Global Initiative for Childhood Cancer (GICC).
- Team members have participated in 11 preparatory meetings for the Global Status Report and 4 special meetings with WHO headquarters to discuss childhood cancer.

- **COVID-19 and Childhood Cancer:** This project evaluates the impact of the COVID-19 pandemic on childhood cancer incidence, referral, diagnosis, and treatment.
- **EPiChildCan:** A project focused on identifying epigenetic precursor markers associated with early-life factors and childhood cancer risk, leveraging large networks of prospective and retrospective studies.
- **International Lifestyle Behaviour and Biobanking Programme in Paediatric Oncology:** A collaboration aimed at developing resources to study the impact of nutrition and lifestyle factors on health outcomes in children with cancer.
- **Global Acute Leukaemia/Lymphoma Network (GALnet):** This consortium enhances collaboration between high-income and low-income countries in paediatric oncology, contributing to improved detection and treatment.
- **Determinants of Late Diagnosis and Delayed Treatment of Cancer (DEDICA):** A study evaluating the factors affecting timely diagnosis and treatment initiation in childhood cancers.
- **IARC Monographs Programme:** Identifying causes of human cancer, including childhood cancers, and evaluating agents associated with cancer risk.
- **South-ROCK:** An integrated center of excellence in paediatric oncology research based in southern France, focusing on therapeutic strategies and environmental factors in cancer prevention.

Applications and grants

Since its establishment, the CCARE Team has successfully secured several grants, totalling more than €1.3 million, including:

- **EpiEarlyCNS:** Funded by the French National Cancer Institute, focusing on epigenomic analyses of paediatric brain cancer.
- **WpCigCAD:** A project investigating the molecular effects of tobacco across life stages.
- **ENV-ALL:** Examining maternal exposure to environmental hazards and its link to acute lymphoblastic leukaemia.
- **CICERO:** Funded by the Dutch Ministry, focusing on childhood cancer in Africa.
- **ChildGICR:** A collaborative programme with St Jude for childhood cancer registration.
- **pLeuk.Fol.WCRF:** Investigating the role of maternal folate's role in childhood leukaemia initiation.

Training

The CCARE Team prioritizes training, with several initiatives including:

- **Online courses:** Training on childhood cancer registration conducted in collaboration with health organizations in Georgia and Trinidad and Tobago.
- **IARC seminar:** Plans for seminar in early 2025 dedicated to childhood cancer research at IARC.
- **Supervision and training:** Ongoing supervision of postdoctoral scientists involved in childhood cancer research.

Key partners

Cooperations across IARC Branches
The CCARE Team collaborates on various publications and projects across different IARC scientific branches:

- **NME, CSU, and LSB**: Publications focusing on early-life nutrition and its relationship to childhood cancer.
- **CSU and ENV**: Collaborative works on childhood cancer incidence statistics.
- **ENV, EGM, and CSU**: The **CICERO** project: Childhood Cancer – Epidemiology, Research, and Omics, funded by the Ministry of Health, Welfare and Sports of the Netherlands.
- **EGM and ENV**: Projects exploring the origins and causes of paediatric cancer (PEDIAC and PEDIAHRG).
- **EGM and CSU**: **South-ROCK** project—Research on Cancer in Kids, funded by INCa, France.
- Collaboration with **WHO** for a side event focused on nutrition and childhood cancer and contributions to the **Global Status Report on Cancer**.

Collaboration with external partners

- The CCARE Team participates in significant events such as the **International Childhood Cancer Day** (celebrated since 2003) on **15 February** and **Childhood Cancer Awareness Month** in September (in 2023 and 2024).
- Collaborations extend to numerous organizations, including:
  - **Union for International Cancer Control (UICC)**
  - **Government of the Netherlands**
  - **French National Cancer Institute (INCa)**
  - **St. Jude Children's Research Hospital (USA)**
  - **Children with Cancer UK**
  - **International Childhood Cancer Cohort Consortium (I4C)**
  - **Childhood Leukemia International Consortium (CLIC)**
  - **Pregnancy and Childhood Epigenetics Consortium (PACE)**
  - **Cancer Research Center of Lyon (CRCL)**
  - **SEER/NCI**

Main innovations

- **Global childhood cancer registration:** Development of a standardized system for childhood cancer registration, enhancing data collection and analysis globally.
- **International initiative for paediatrics and nutrition:** Investigating the influence of diet, obesity, and metabolic health on childhood cancer, particularly in LMICs.
- **Environmental risk factors:** Studying links between exposure to magnetic fields from power lines and childhood leukaemia, as well as parental pesticide exposure.
- **Molecular causes of childhood cancer:** Exploring the effects of maternal and paternal age, adiposity during pregnancy, and lifestyle factors on cancer risk in children.
- **Indicators of cancer burden:** Developing indicators tailored for childhood populations to assess the global burden of childhood cancer.
- **Economic impact analysis:** Evaluating the financial impact of childhood cancer on families in LMICs.

Contributions to MTS implementation

The CCARE Team's activities align with the MTS 2021-2025, contributing to:
Fundamental priorities:

- ➔ **Data for action:** Collection and analysis of childhood cancer incidence and survival data.
- ➔ **Understanding causes:** Investigating epidemiological and molecular risk factors.
- ➔ **From understanding to prevention:** Identifying biomarkers for early detection.
- ➔ **Knowledge mobilization:** Supporting research and capacity building in LMICs.

Emerging priorities:

- ➔ **Evolving cancer risk factors:** Addressing childhood cancer research in LMIC populations.
- ➔ **Implementation research:** Assisting WHO's GICC in reducing the childhood cancer burden.

Main challenges

- **Diverse research themes:** The wide scope of research makes it challenging to produce comprehensive grant applications and publications.
- **Need for data management:** Developing reliable data management strategies and trusted collaborations with data providers is essential for effective research.
- **Funding and sustainability:** The Team faces challenges in securing long-term funding and maintaining momentum in its initiatives.

Next steps

To advance its objectives, the CCARE Team plans to:

- ➔ **Communication campaign:** Launch a campaign in September 2024 to highlight childhood cancer research, with a dedicated webpage to showcase activities and results.
- ➔ **Support GICC:** Develop an action plan to assist with the Global Status Report, ensuring effective communication of IARC's contributions.
- ➔ **Stimulate scientific exchange:** Organize an IARC seminar on childhood cancer and foster collaborative publications.
- ➔ **Implementation support:** Create lay publications, evidence summaries, and training courses tailored for a general audience.
- ➔ **Resource mobilization:** Actively seek funding opportunities and collaborate with IARC's Resource Mobilization Office.

RECOMMENDATIONS

The CCARE Team should focus on:

- ✓ Proposing methods for managing and disseminating data tailored to sparse information environments.
- ✓ Concentrating on research projects that explore poorly understood risk factors, crucial for developing prevention programmes.
- ✓ Strengthening collaboration with WHO and supporting GICC by leveraging the expertise across all IARC pillars (1, 2, 3, and 4).

Key publications

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- Targeting childhood cancer through Global Initiative for Cancer Registry Development (ChildGICR)
- Cancer Risk in Childhood Cancer Survivors (CRICCS)
- EPiChildCan project
- WHO Classification of Tumours - Paediatric tumours
- WHO Global Initiative for Childhood Cancer

Gastric Cancer Prevention (GCP) Team

Members

Team leaders: Dr Jin Young Park (Scientist, EPR)

Team members: The GCP Team comprises 11 team members from 4 Branches in Pillars 1, 2 and 3.

➔ Dr Isabelle Soerjomataram (Deputy Branch Head, CSU); Dr Eileen Morgan (Scientist, CSU); Dr Behnoush Abedi-Ardekani (Scientist, GEM); Dr Mazda Jenab (Scientist, NME); Dr Pekka Keski-Rahkonen (Scientist, NME); Dr Sabina Rinaldi (Deputy Branch Head, NME); Ms Viktoria Knaze (Research Project Associate, EPR); Dr Gary Clifford (Deputy Branch Head, EPR); Dr Iacopo Baussano (Scientist, EPR); Dr Partha Basu (Branch Head, EPR).

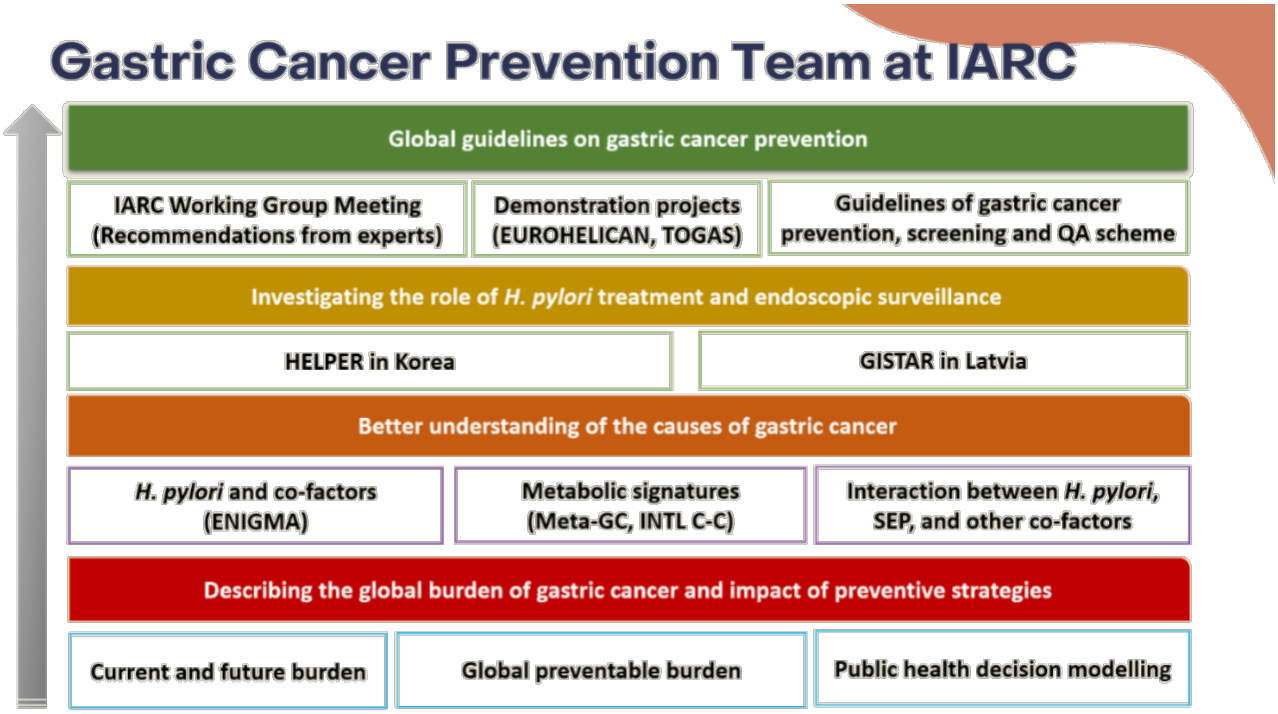
Cancer types Teams
➔ Starting date: October 2022

Objectives

The primary aim of the GCP Team is to mitigate the global burden of gastric cancer. The team seeks to produce robust evidence to enhance the understanding of its causes, assess the efficacy and effectiveness of population-based interventions and prevention programmes, and ultimately implement evidence-based strategies for the prevention and control of gastric cancer. The GCP Team is committed to supporting the practical application of these strategies worldwide through cross-agency and international collaborations.

Research focus

With projections indicating a significant increase in the future global burden of gastric cancer, and recognizing its substantial contribution to cancer disparities in various regions, there is a compelling need for intense research into gastric cancer etiology and prevention. The GCP Team's diverse range of activities spans from etiological research aimed at identifying novel biomarkers of metabolic perturbations to randomized controlled clinical trials focused on primary and secondary prevention, as well as demonstration projects for *Helicobacter pylori* test-and-treat programmes. This comprehensive approach will not only showcase IARC's gastric cancer prevention efforts but also foster opportunities for new collaborations.



Workplan Themes

As summarized in the chart above, the workplan of the GCP Team focuses on four main themes:

1. Describing the current and future burden of gastric cancer (Project Tree 1).
2. Understanding risk factors in diverse populations with varying gastric cancer risks using standardized multicenter protocols (Project Tree 2).
3. Investigating the role of H. pylori treatment and endoscopic surveillance in preventing gastric cancer in high-incidence areas (Project Tree 3).
4. Implementing population-based H. pylori test-and-treat strategies and endoscopic screening in high-risk populations to prevent gastric cancer and reduce inequalities associated with the disease (Project Tree 4).

Governance

The governance of the GCP Team is led by Dr Jin Young Park, with daily project management overseen by Ms Viktoria Knaze. The Team conducts regular meetings with its members and engages in cross-agency meetings focused on specific projects, including HELPER, GISTAR (as part of EUROHELICAN), EU Guidelines, TOGAS, ENIGMA, Meta-GC, and INTL-CC.

In addition, the GCP Team collaborates with other IARC Research Teams, such as the Oesophageal Cancer (ECA) Team, Hormones and Metabolism (HorM) Team, Onco-Metabolomics (OMB) Team, and Public Health Decision Science (PHDS) Team.

Collaboration with WHO

Currently, the GCP Team does not have any collaborations with WHO (either headquarters or regional offices). However, the Team plans to engage with WHO headquarters when appropriate to promote a WHO Global Initiative on Gastric Cancer Elimination.

Workplan progress

Projects and consortia

The GCP Team coordinates or directly contributes to nine international projects, which are geographically diverse and currently ongoing. These projects include:

- **ATLAS HP**
- **ENIGMA**
- **Meta-GC**
- **INTL-CC**
- **HELPER**
- **GISTAR**
- **EUROHELICAN**
- **TOGAS**
- **European Guidelines**

Through these consortia, GCP Team members have established collaborations across all five continents.

Applications and grants

The GCP Team conducts its activities with support from three active grants, sourced from INCa, the European Commission (EC), and GCSF:

- **Exploring metabolic disturbances:** Investigating metabolic disturbances associated with gastric cancer development by comparing French, European, and high-risk populations. Funded by the Institut National du Cancer (€331 232 total).
- **EUROHELICAN:** Accelerating gastric cancer reduction in Europe through Helicobacter pylori eradication, funded by the European Commission (€1 million total).
- **HELPER:** Funded by GCSF (€1 million total).

The GCP Team is also anticipating confirmation of two additional grants:

- **NIH grant:** " Circulating Metabolites as Novel Risk Biomarkers for Gastric Cancer" – a large multicentre prospective investigation, totalling US$ 4.3 million.
- **European Commission grant:** "European Guidelines on Gastric Cancer Prevention, Screening, Diagnosis, and Quality Assurance Scheme," totalling €2 million.

Key collaborations

Cooperation across IARC Branches
The GCP Team, led by the EPR Branch within Pillar 3, relies on collaborations with Pillar 1 (CSU) and Pillar 2 (GEM and NME). At this stage, the team does not include participants from Pillar 4. Although some training programmes are conducted by the GCP Team members, they currently lack support from the LCB Branch. Initial contacts have been made with the ESC Branch to discuss the preparation of an IARC Handbook focused on cancer prevention related to gastric cancer.

Collaboration with External Partners
The GCP Team collaborates with several key scientific partners, including:

- **HELPER**: National Cancer Center of Korea and 11 major university hospitals in the Republic of Korea.
- **GISTAR**: University of Latvia.
- **ENIGMA**: Pontificia Universidad Católica de Chile (Chile); Tehran University of Medical Sciences (Islamic Republic of Iran); Ardabil University of Medical Sciences (Islamic Republic of Iran); MRC/UVRI and LSHTM Uganda Research Unit (Uganda); University of Zambia School of Medicine (Zambia); University of Otago (New Zealand)
- **Meta-GC**: INSERM and Gustave Roussy (France), along with EPIC collaborators.
- **INTL-CC**: Memorial Sloan Kettering Cancer Center (USA).
- **EU Project EUROHELICAN**: Collaborations with partners in Slovenia, Latvia, and France.
- **EU Project TOGAS**: Collaborations with multiple countries including Latvia, Austria, Belgium, Croatia, France, Germany, Ireland, Lithuania, the Netherlands, Poland, Portugal, Romania, Slovenia, and Spain.

Training

Since its establishment, the GCP Team has participated in several training sessions, including:

- Project management in Global Health: Provided by the University of Washington.
- WHO project management course
- International conference on harmonisation guidelines, good clinical practice training: Whitehall training.
- Human research protection training: Conducted with the United States Department of Health and Human Services.

Main innovations

The IARC GCP Team has established itself as a **global reference for gastric cancer** prevention, as evidenced by its active participation in several international consortia and its leadership role in developing global guidelines. The Team's work highlights that the incidence of gastric cancers is expected to continue increasing over the next decades. Addressing disparities in gastric cancer remains a critical issue that requires global action. In low-resource settings, cancer treatment is often both unavailable and unaffordable, making prevention and early detection essential for effective cancer control. There is a pressing need for more data and improved strategies to implement prevention programmes for gastric cancer, even in areas with low to intermediate risk, to combat disparities in gastric cancer. It is important to note that screening is not a panacea for cancer control, because it can lead to wasted resources and potential harm.

Contributions to MTS implementation

Fundamental priorities

The work programme of the GCP Team aligns seamlessly with the priorities of the MTS, addressing all of IARC's fundamental priorities:

- ➔ **Pillar 1:** Determining who gets gastric cancer, where, and when (e.g. ATLAS HP).
- ➔ **Pillar 2:** Understanding the causes of gastric cancer (e.g. ENIGMA, Meta-GC, INTL-CC).

- ➔ **Pillar 3:** Evaluating various preventive strategies and implementing the best evidence-based approaches (e.g., HELPER, GISTAR, EUROHELICAN, TOGAS)
- ➔ **Pillar 4:** Actively participating in dissemination activities related to gastric cancer prevention (e.g., EUROHELICAN, TOGAS, IARC Working Group meeting).

Main challenges

Accelerating the reduction of gastric cancer and eliminating disparities presents a significant public health challenge. Unfortunately, gastric cancer remains neglected, with limited resources allocated both internally and externally. There is a long-held misconception that this cancer will resolve on its own. The GCP Team believes that the continuity of some projects is at risk due to limited staffing. In this context, the Team's ambitions include:

- Positioning gastric cancer: Advocating for gastric cancer to be the next focus for a WHO's global cancer initiative.
- Raising awareness: Drawing renewed attention to this neglected but major public health burden.

Next steps

The GCP Team has outlined the following next steps for the continued development of the Research Team:

- ➔ **IARC Working Group meeting:** Organize a meeting focused on best practices for implementing population-based H. pylori test-and-treat strategies, with the aim of disseminating the IARC Working Group Report in 2025 (as part of EUROHELICAN).
- ➔ **Confirmation of prevention strategies:** Validate the effectiveness of various prevention strategies within the next two years through rigorously conducted randomized controlled clinical trials (e.g., HELPER, GISTAR).
- ➔ **Development of EU guidelines:** Prepare for the creation of gastric cancer European guidelines and quality assurance schemes.
- ➔ **Collaborations:** Foster active collaborations with the Joint Research Centre (JRC) and European experts.
- ➔ **Expansion of metabolomics:** Increase metabolomics research efforts in the USA and the Republic of Korea.
- ➔ **Utilization of ENIGMA resources:** Leverage opportunities for expanding collaborations using ENIGMA resources.
- ➔ **Staff recruitment:** Fill positions with new grants, including Scientist, Project Officer/Scientist, and Project Assistant roles.

RECOMMENDATIONS

The GCP Team's contributions to the implementation of IARC's MTS for cancer prevention are commendable, and the Research Team deserves greater visibility. Therefore, the GCP Team is encouraged to:

- ✓ Draft a position paper in 2025-2026 as an outcome of the international meeting scheduled at IARC in February 2025.
- ✓ Produce an IARC Evidence Summary Brief in 2025 to initiate discussions with WHO headquarters.
- ✓ Collaborate with the ESC Branch to prepare a framework for producing an *IARC Handbook* on the prevention of gastric cancer.

Key publications

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IARC Cervical Cancer Elimination Initiative (CCEI) Team

Members

Team leaders: Dr Mary Luz Rol (Scientist and Team leader, EPR) and Dr Partha Basu (Branch Head and co-Team leader; EPR)

10 team members from 4 Branches in Pillars 1, 3 and 4:

- Dr Freddie Bray (Branch Head; CSU); Dr Ariana Znaor (Scientist; CSU); Dr Gary Clifford (Deputy Head; EPR); Mr Eric Lucas (Scientist; EPR); Dr Iacopo Baussano (Scientist; EPR); Dr Tatiana Ramirez (Postdoctoral Scientist; EPR); Dr Tarik Gheit (Scientist, EGM) invited to participate as member, September 2024); Dr Gabrielle Goldman Levy (Pathologist; ESC); Mrs Anouk Berger (Branch Head; LCB)

Cancer types Teams
➔ Starting date: April 2023

Objectives

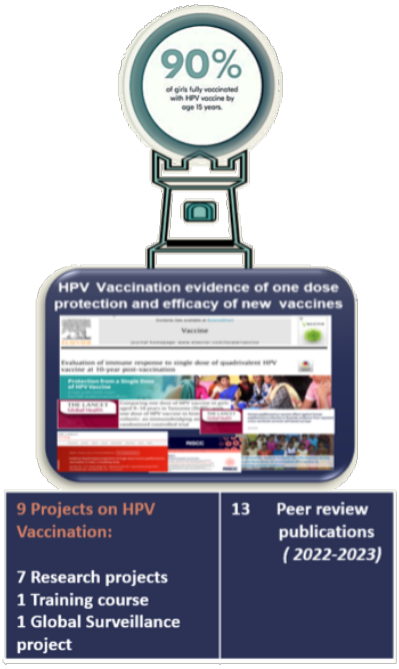
Context

Cervical cancer primarily results from persistent infection with high-risk types of human papillomavirus (HPV), a highly prevalent virus transmitted through sexual contact. Although cervical cancer is one of the most preventable and treatable cancers, an estimated 604 000 women were diagnosed globally in 2020, resulting in about 342 000 deaths, and 90% of cases and deaths occurred in LMICs.

In November 2020, WHO launched the Global Strategy to Accelerate the Elimination of Cervical Cancer. This strategy is built on three strategic pillars with specific targets:

- Vaccination: 90% of girls fully vaccinated with the HPV vaccine by age 15 years.
- Screening: 70% of women screened with a high-performance test by ages 35 and 45 years.
- Treatment: 90% of women with precancer treated and 90% of women with invasive cancer managed.

To achieve these 90–70–90 targets by 2030, IARC supports the WHO initiative by providing crucial evidence, technical materials, and updates for policymakers and programme managers.



9 Projects on HPV Vaccination:	13 Peer review publications *(2022-2023)*
7 Research projects 1 Training course 1 Global Surveillance project	

21 Projects on Cervical cancer Screening:	25 Peer review publications *(2022-2023)*
14 Research projects 1 Communication report 5 Training courses 1 Global Surveillance project	

11 Projects on Cervical cancer treatment:	7 Peer review publications *(2022-2023)*
5 Research projects 1 Communication report 4 Training courses 1 Global Surveillance project	

The IARC CCEI Team was established to enhance communication and coordination with the WHO Cancer Team and to facilitate knowledge and expertise exchange related to the CCEI. The primary goal of the IARC CCEI Team is to foster collaboration among CCEI partners, including WHO, while sharing scientific evidence and updates on relevant IARC initiatives and publications.

Research focus

IARC Team members are conducting research in three key areas within the CCEI framework. The CCEI Team's workplan includes:

- ➔ Studying immune responses to and effectiveness of one dose of the HPV vaccine compared with two and three doses.
- ➔ Evaluating the feasibility and effectiveness of various cervical cancer screening methods.
- ➔ Assessing the safety and effectiveness of novel precancer treatment methods and evaluating real-world effectiveness through implementation research.

Workplan progress

Projects and consortia

The CCEI Team manages 41 ongoing research and capacity-building projects, categorized as follows:

- 9 projects related to vaccination
- 21 projects related to screening
- 11 projects related to treatment and cancer incidence

Applications and grants

The CCEI Team has successfully secured the following grants:

- **HPV Vaccine Effectiveness Coordination Center**

Funder: Bill & Melinda Gates Foundation
IARC Budget: €4,299,652 (Direct funding)
IARC PI: Dr Iacopo Baussano (Coordinator)

- **Measurement of Human Papillomavirus (HPV) Vaccine Introduction Impact**

Funder: WHO headquarters
IARC Budget: €1,295,072 (Direct funding)
IARC PI: Dr Iacopo Baussano (Partner)

- **HPV Self-Sampling in the General Population: Efficacy, Feasibility, Acceptability, and Cost-Effectiveness (MIRABELLE)**

Funder: Institut National du Cancer (INCa FR)
IARC Budget: €400,246 (Regular grant)
IARC PI: Dr Catherine Sauvaget (Coordinator)

In addition to these three grants, two applications are currently under review by the European Commission (project HPV FASTER IMPLEMENT) and NIH (HPV circulating DNA as a pre-diagnostic marker for anal and other HPV-related cancers in individuals living with HIV).

Governance

The CCEI Team meets regularly to coordinate efforts, discuss priorities, and strategize grant applications. Team members also serve on steering committees for various collaborative projects at IARC focused on cervical cancer prevention.

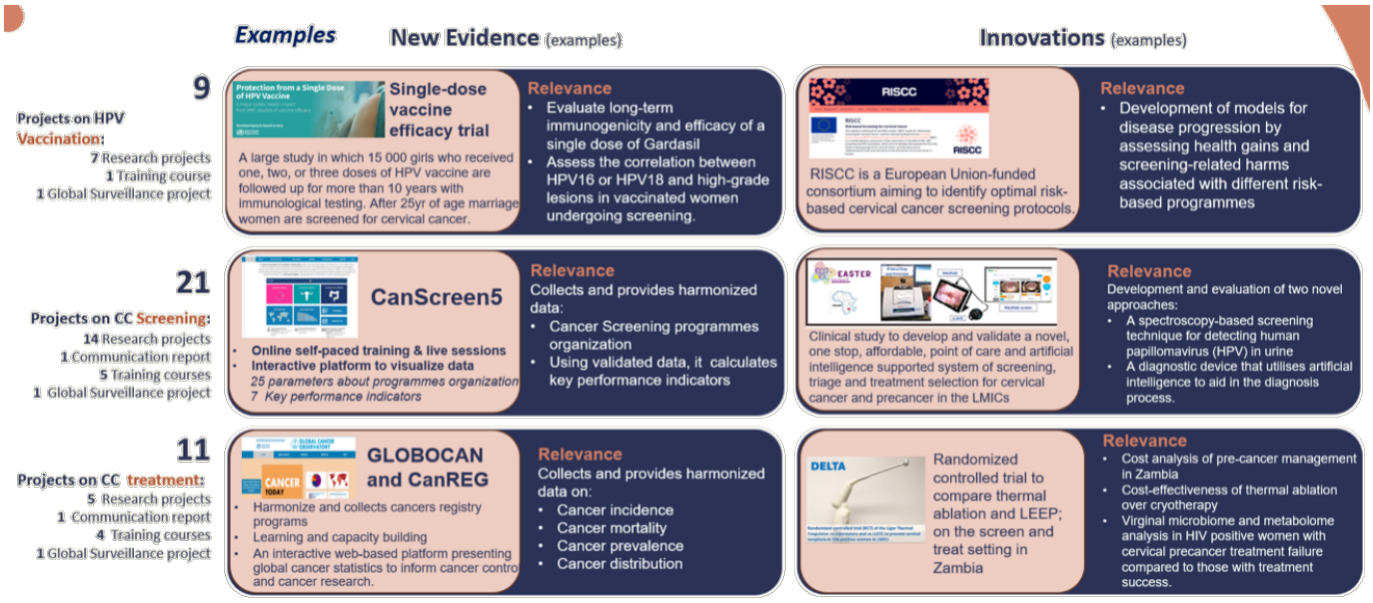
Links with WHO

The CCEI Team collaborates closely with WHO, specifically with Dr Bente Mikkelsen, the Director of the Noncommunicable Diseases Division at WHO headquarters. This partnership extends to WHO regional offices, including those of the Americas (PAHO), Africa (AFRO), and South-East Asia (SEARO). To support this collaboration, the CCEI Team has shared a comprehensive database of 41 IARC projects with WHO, accompanied by summary presentations of each project. These initiatives are also featured in the WHO Cervical Cancer Elimination Initiative Knowledge Repository.

The CCEI Team actively participates in various WHO CCEI activities and events, including:

- The commemoration on 17 November 2023.
- The CCEI stakeholder online meeting on 4 December 2023.
- The CCEI stakeholder meeting in Cartagena, Colombia, on 5–8 March 2024.

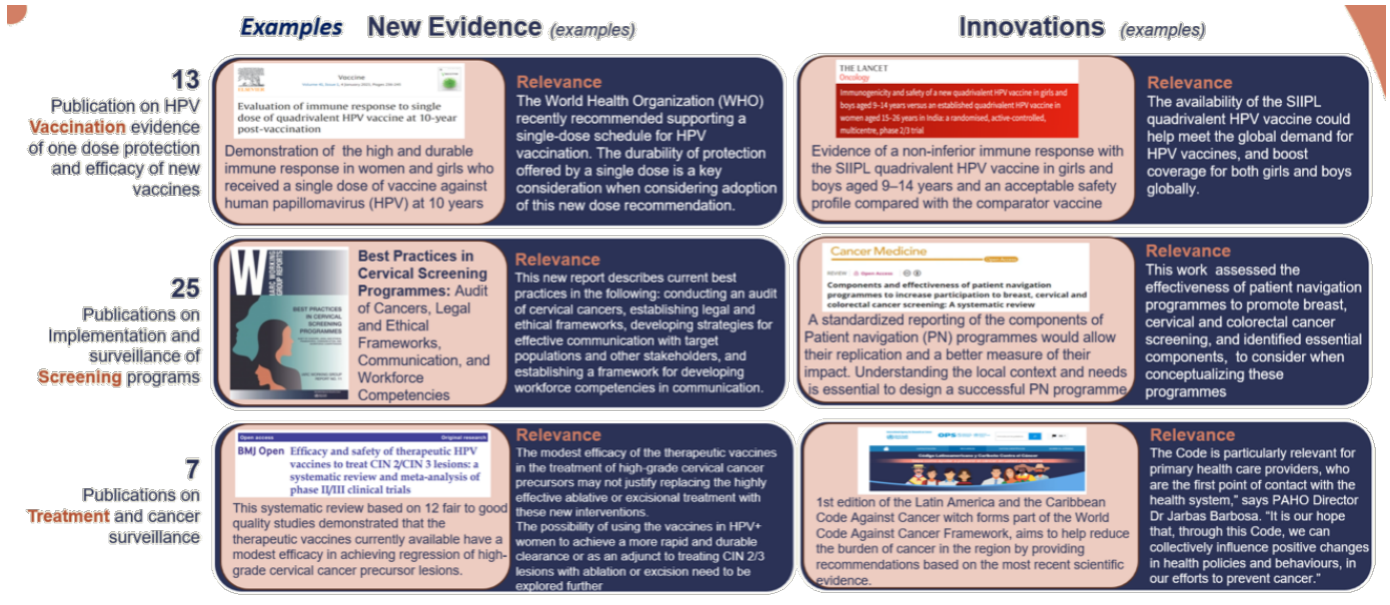
Furthermore, the CCEI Team contributes to training programmes for the WHO Academy. A massive hybrid learning programme on cervical screening and management, developed with technical support from IARC, is set for release by the end of 2024.



Publications

The CCEI Team has produced 45 publications on HPV and cervical cancer (see "Key publications" below), including:

- 13 on HPV vaccination
- 25 on screening programmes
- 7 on treatment and cancer surveillance.



Training

The CCEI Team is developing extensive training materials on cervical cancer, including the HPV atlas to support cervical cancer elimination (see "References" below) and presentations for the IARC Summer School. The Team collaborates with the International Federation for Cervical Pathology and Colposcopy (IFCPC) on training initiatives. Notably, Team members contributed to one of the first courses offered by the WHO Academy in 2020: "Comprehensive Learning Programme on Screening, Diagnosis, and Management of Cervical Precancer".

Main innovations

One significant strength of the CCEI Team is its ability to leverage extensive data from LMICs to create relevant models that are not solely based on perspectives from HICs. This approach aids WHO in defining meaningful targets and clear messages for governments in LMICs.

Key innovations from the CCEI Team include:

- Single-dose HPV vaccine study: An important IARC study demonstrating that a single dose of the HPV vaccine provides adequate protection against the virus, with high immunogenicity persisting for at least 10 years. Based on these findings, WHO recently recommended the adoption of a single-dose vaccination schedule.

- Cervical cancer screening evaluation: The CCEI Team is evaluating the feasibility and effectiveness of various cervical cancer screening methods. The IARC Handbooks of Cancer Prevention Volume 18: Cervical Cancer Screening was published in May 2022.

- Performance assessment of VIA: A recent IARC study assessed the performance of visual inspection of the cervix with acetic acid (VIA), a low-cost screening method, and evaluated the ability of VIA providers to determine eligibility for ablative treatment.

Key collaborations

Collaborations across Branches
Under the leadership of the EPR Branch in Pillar 3, the CCEI Team collaborates with Pillar 1 (CSU) for cervical cancer data, as well as Pillar 3 (ESC and LCB). The CCEI Team has worked with the ESC Branch on the IARC Handbooks programme (Handbook on Cervical Cancer Screening) and the Blue Books programme (WHO Classification of Tumours: Female Genital Tumours). In addition, the Team is heavily involved in training programmes and collaborates closely with the LCB Branch.

External collaborations
In addition to WHO, key partners for the CCEI Team include the Bill & Melinda Gates Foundation (BMGF), the United States National Cancer Institute (NCI/NIH), and the European Commission. BMGF provides significant funding for several of the CCEI Team's projects, totalling several million US dollars (see Workplan progress on projects and grants).

Contributions to MTS implementation

IARC's contributions to the WHO Global Strategy to Accelerate the Elimination of Cervical Cancer are prioritized in the MTS 2021-2025, stating that "IARC contributes to the implementation of the WHO Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem through r e-evaluating the effectiveness of cervical cancer screening; monitoring and evaluating cervical cancer elimination in sub-Saharan Africa; assessing HPV vaccination interventions in various countries; and evaluating the effectiveness of cervical cancer screening and treatment programmes for precancerous lesions. Over the next five years, IARC will assess the efficacy and effectiveness of HPV vaccination programmes (including reduced dosing schedules) in diverse implementation scenarios. The generated evidence will support health authorities in deploying mass HPV vaccination initiatives."

Fundamental priorities

The workplan of the CCEI Team directly addresses three fundamental priorities of the MTS 2021-2025:

- ➔ **Data for action:** Providing estimates of cervical cancer incidence and mortality and maintaining the CCEI Knowledge Repository.
- ➔ **From understanding to prevention:** Conducting projects on HPV vaccination and implementation research on screening and treatment.
- ➔ **Knowledge mobilization:** Developing the *IARC Handbooks of Cancer Prevention* volume on Cervical Cancer Screening, the Atlas on cervical cancer, and training materials, including courses for the WHO Academy.

Main challenges

According to the CCEI Team leaders, the primary challenges for the CCEI Team include:

- **Communication:** Ensuring regular communication with the WHO NCD department and maintaining centralized communication with WHO.
- **Resource mobilization:** Securing funding to support IARC's participation in CCEI events.

Next steps

The CCEI Team identifies the following next steps for developing the CCEI Team:

- ➔ Continue coordinating internal communication on CCEI within IARC.
- ➔ Work on defining IARC's vision for the CCEI.
- ➔ Maintain active participation in WHO activities related to the CCEI

RECOMMENDATIONS

- ✓ The scientific output of the CCEI Team provides an excellent foundation for developing models and cost-benefit analyses of cancer prevention programmes. Projects led by Dr Iacopo Baussano, supported by CSU data, should enable IARC to pursue new ambitions in health economics, using cervical cancer as a pilot project.
- ✓ The CCEI Team exemplifies effective collaboration with WHO on the initiative to eliminate cervical cancer. In March 2024, WHO announced significant investments in CCEI, amounting to a US$ 600 million budget. This funding includes US$ 400 million from the World Bank, US$ 180 million from the Bill & Melinda Gates Foundation, and US$ 10 million from UNICEF. The CCEI Team should establish the appropriate interface with WHO in light of this new ambition.

Key publications

Key publications on HPV vaccination:

- Joshi S, Anantharaman D, Muwonge R, Bhatla N, Panicker G, Butt J, et al. (2023). Evaluation of immune response to single dose of quadrivalent HPV vaccine at 10-year post-vaccination. Vaccine. 41(1):236–45. PMID:36446654
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- Schuind AE, Rees H, Schiller J, Mugo N, Dull P, Barnabas R, et al. (2023). State-of-the-science of human papillomavirus vaccination in women with human immunodeficiency virus: summary of a scientific workshop. Prev Med Rep. 35:102331. PMID:37576844
- Man I, Georges D, de Carvalho TM, Ray Saraswati L, Bhandari P, Kataria I, et al. (2022). Evidence-based impact projections of single-dose human papillomavirus vaccination in India: a modelling study. Lancet Oncol. 23(11):1419–29. PMID:36174583
- Man I, Georges D, Sankaranarayanan R, Basu P, Baussano I (2023). Building resilient cervical cancer prevention through gender-neutral HPV vaccination. Elife. 12:e85735.

Key publications on cervical cancer screening and surveillance:

- IARC (2022). Cervical cancer screening. IARC Handbooks Cancer Prev. 18:1–456.
- IARC; Department of Health and Health Service Executive of Ireland (2023). Best practices in cervical screening programmes: audit of cancers, legal and ethical frameworks, communication, and workforce competencies. Lyon, France: International Agency for Research on Cancer (IARC Working Group Reports, No. 11). Licence: CC BY-NC-ND 3.0 IGO.
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- Mallafré-Larrosa M, Ritchie D, Papi G, Mosquera I, Mensah K, Lucas E, et al.; CBIG-SCREEN Consortium (2023). Survey of current policies towards widening cervical screening coverage among vulnerable women in 22 European countries. Eur J Public Health. 33(3):502–8.

Cervical cancer treatment and surveillance:

- WHO Classification of Tumours Editorial Board (2020). Female genital tumours. 5th ed. Lyon, France: International Agency for Research on Cancer (WHO Classification of Tumours series, Vol. 4).
- IARC and PAHO (2023). Latin America and the Caribbean Code Against Cancer. 1st ed. Lyon, France: International Agency for Research on Cancer; Washington (DC), USA: Pan American Health Organization.
- Singh D, Vignat J, Lorenzoni V, Eslahi M, Ginsburg O, Lauby-Secretan B, et al. (2023). Global estimates of incidence and mortality of cervical cancer in 2020: a baseline analysis of the WHO Global Cervical Cancer Elimination Initiative. Lancet Glob Health. 11(2):e197–206. PMID:36528031
- Ibrahim Khalil A, Zhang L, Muwonge R, Sauvaget C, Basu P (2023). Efficacy and safety of therapeutic HPV vaccines to treat CIN 2/CIN 3 lesions: a systematic review and meta-analysis of phase II/III clinical trials. BMJ Open. 13(10):e069616. PMID:37879679

- Zhang L, Sauvaget C, Mosquera I, Basu P (2023). Efficacy, acceptability and safety of ablative versus excisional procedure in the treatment of histologically confirmed CIN2/3: a systematic review. BJOG. 130(2):153–61. PMID:35689493

References

- Webpage of the CCEI Team
- HPV atlas to support cervical cancer elimination
- IARC Handbook of Cancer Prevention on Cervical Cancer Screening
- IARC Evidence Summary Brief, titled “Protection from a Single Dose of HPV Vaccine: A major public health impact from IARC studies of vaccine efficacy”
- Global estimates of incidence and mortality of cervical cancer in 2020
- WHO Classification of Tumours: Female Genital Tumours
- WHO Cervical Cancer Elimination Initiative

IARC Global Breast Cancer Initiative (GBCI) Team

Cancer types Teams
➔ Starting date: 2023

Members

Team leaders: Dr Nadya Dimitrova (Public Health Officer), Early Detection, Prevention, and Infections Branch (EPR) and Dr Marion Piñeros (Scientist), Cancer Surveillance Branch (CSU)

Team members: The GBCI Team comprises 9 Team members (9 scientists including one postdoctoral scientist) from 3 Branches in IARC Pillars 1 (CSU) and 3 (EPR and ENV).

➔ Dr Freddie Bray (Branch Head; CSU); Dr Partha Basu (Branch Head, EPR); Dr Andre Carvalho (Scientist, EPR); Dr Isabel Mosquera (Scientist, EPR); Dr Farida Selmouni (Scientist, EPR); Dr Valerie McCormack (Deputy Branch Head, ENV); Dr Carolina Espina (Scientist, ENV); Dr Milena Foerster (Scientist, ENV); Dr Pauline Boucheron (Postdoctoral Scientist, ENV)

Objectives

Context

IARC and WHO have complementary functions and mandates aimed at advancing global cancer control. On 8 March 2021, WHO launched the Global Breast Cancer Initiative (GBCI) with the goal of reducing breast cancer mortality by 2.5% annually. To achieve this objective, three key pillars and specific targets were established:

- **Pillar 1:** Health promotion for early detection
  Target: Achieve a diagnosis of at least 60% of invasive cancers at stages I or II.
- **Pillar 2:** Timely diagnosis
  Target: Complete evaluation, imaging, tissue sampling, and pathology within 60 days.
- **Pillar 3:** Comprehensive breast cancer management
- **Target:** Ensure that at least 80% of patients with breast cancer receive a full course of multimodal treatment and successfully return home.

In this context, the objectives of the IARC GBCI Team are:

1. **Facilitating communication:** The primary aim of the IARC GBCI Team is to enhance coordination and communication between the WHO and IARC GBCI teams, sharing scientific evidence, expertise, and updates on relevant IARC initiatives and publications.
2. **Information sharing:** The overall objective is to disseminate information and updates on the latest developments concerning ongoing IARC projects, including sharing insights with WHO and fostering dialogue among IARC groups working on breast cancer initiatives.

The Team's activities, aligned with the GBCI pillars, include:

➔ **Development and dissemination of supporting data and tools:**

- Estimation of breast cancer burden via the IARC Global Cancer Observatory, which provides information on incidence, mortality, and prevalence for 185 countries or territories.
- Analysis of breast cancer mortality trends by age in 70 middle- and high-income countries (accessible via the Cancer Over Time subsite of the Global Cancer Observatory).
- Reporting of cancer incidence data from high-quality cancer registries worldwide through the periodic publication Cancer Incidence in Five Continents.
- Support for cancer registries in less-developed settings via the Global Initiative for Cancer Registry Development (GICR).
- Collection of breast cancer incidence and survival data by stage and age in about 70 LMICs (SURVCAN-4).
- Estimation of breast cancer prevalence according to phases of care (PrevPhase-1).
- Assessment of the intergenerational impact of premature deaths from breast cancer, specifically concerning maternal orphans.
- Cancer Screening in Five Continents (CanScreen5).

- Development of the World Code Against Cancer Framework and related educational materials for health promoters and frontline health-care professionals.
- Launch of the IARC Learning Portal, including a self-paced learning programme on improving the quality of cancer screening.
- Creation of a digital atlas on clinical breast examination (CBE), diagnostic mammography, breast ultrasound, and breast pathology (Atlas of Breast Cancer Early Detection).
- Development of country-specific breast cancer profiles within the GBCI framework (e.g., Namibia).
- Data collation at IARC to support GBCI pillar key performance indicators (KPIs).

Governance

Meetings commenced in March 2023 with Dr Benjamin Anderson from WHO Headquarters. As of January 2024, these meetings have continued with Dr Mary Nyangasi, Technical Officer for Cancer in the Department of Non-Communicable Diseases, Disability, and Rehabilitation at headquarters/UCN/NCD/MND in Geneva, Switzerland. Dr Nyangasi serves as the WHO headquarters focal point for the WHO GBCI. A technical working group comprising international partners has been established by WHO, which includes participation from IARC GBCI members.

Links with WHO
The GBCI Team maintains a close cooperative relationship with WHO on the WHO GBCI, with Dr Mary Nyangasi as the primary contact at WHO headquarters.

➔ **Pillar 1: Health promotion for early detection**

- Development of standards and recommendations regarding breast cancer incidence by stage at diagnosis at the population level.
- Implementation of the World Code Against Cancer Framework and creation of educational materials for health promoters and front-line health-care professionals.
- Establishment of a digital atlas on clinical breast examination (CBE), diagnostic mammography, breast ultrasound, and breast pathology (Atlas of Breast Cancer Early Detection).
- Conducting studies on the patient journey to diagnosis, health system barriers to early detection, and breast cancer awareness levels in LMICs, including sub-Saharan Africa (e.g., ABC-DO study in Namibia, Nigeria, South Africa, Uganda, and Zambia) and Eastern Europe and Asia (e.g. DEDICA multi-country study).
- Evaluation of clinical breast examination (CBE) through a randomized trial.
- Implementation of a multilevel strategy to improve access to early detection and subsequent care for vulnerable rural populations in India (Access Cancer Control India; ACCI).

➔ **Pillar 2: Timely diagnosis**

- Conducting an IARC multicenter study to evaluate novel technologies aimed at improving early breast cancer diagnosis in resource-limited settings in India and Uganda.
- Creation of a digital atlas on clinical breast examination (CBE), diagnostic mammography, breast ultrasound, and breast pathology (Atlas of Breast Cancer Early Detection).

➔ **Pillar 3: Comprehensive breast cancer management**

- Conducting patterns-of-care studies for breast cancer in Morocco, Nepal, Eastern Europe and Asia (e.g. DEDICA multi-country study), and sub-Saharan Africa (e.g., ABC-DO). This includes interventions aimed at improving treatment completion rates.

Workplan progress

Projects and consortia

- **Webpage development:** The team is in the process of creating a webpage summarizing relevant IARC projects organized by GBCI pillar, which will include supporting data and tools on the three pillars of the WHO initiative.

Key collaborations

Cooperation across IARC Branches
The GBCI Team is primarily led by CSU and EPR Branches, which fall under IARC Pillars 1 and 3. The team collaborates with Pillar 1 (CSU) to gather data on breast cancer and engages with Pillar 3 (EPR and ENV) for related efforts. Currently, the Team does not include participants from Pillars 2 and 4.

- **Resource communication:** The team is responsible for informing the WHO contact person about available resources, including:
  - Data for monitoring breast cancer burden, including stage distribution.
  - Training and capacity-building resources related to TNM classification and screening.
- **Screening and cancer care organization:** Since June 2024, the team has participated in WHO GBCI Technical Working Groups focusing on:
  - The WHO Global Status Report on Cancer.
  - Health Systems Strengthening.
  - Advocacy and Leadership.

Applications and grants
No reported applications or grants related to the GBCI Team during the period of 2023-2024.

Main innovations

- Establishment of an IARC research team formed in alignment with the WHO Global Breast Cancer Initiative.
- Development and dissemination: Focused on creating and distributing supporting data and tools.
- Contribution to WHO Global Initiative pillars through various projects.

Contributions to MTS implementation

IARC's contributions to WHO's Global Initiatives on Cancer are recognized as a priority in the MTS 2021-2025 and are integrated into the IARC-WHO strategic workplan for 2023-2025.

Fundamental priorities
The workplan of the GBCI Team directly addresses two fundamental priorities of the MTS 2021-2025:

- ➔ **Data for action:** Providing estimates of breast cancer incidence, mortality, staging at diagnosis, and projections for 2022-2050.
- ➔ **From understanding to prevention:** Engaging in projects that contribute to the three pillars of the WHO Global Breast Cancer Initiative.

Main challenges

No challenges reported at this time.

Next steps

The GBCI Team has outlined the following next steps for the development of the Team:

- ➔ **Enhance communication:** Strengthen and maintain regular communication with the WHO team responsible for the GBCI.
- ➔ **Identify collaboration topics:** Explore specific topics for collaboration while investigating the availability of funding.
- ➔ **Coordinate efforts:** Complement existing efforts on similar projects to avoid duplication of work.

RECOMMENDATIONS

As a newly established Team, there is room for improvement in terms of structure and organization:

- ✓ This team addresses a specific need within IARC by facilitating communication between IARC and WHO for the implementation of the WHO GBCI. Meetings between the IARC Team and WHO commenced in January 2024 with the new WHO contact person.
- ✓ The team should actively explore grant opportunities and seek direct funding from WHO headquarters.
- ✓ In the medium term, Team leaders are encouraged to consider consolidating IARC initiatives related to breast cancer, including the team on hormones and breast cancer led by Dr Sabina Rinaldi and Dr Laure Dossus, as well as the Working Group on Breast Cancer. This consolidation could optimize knowledge sharing and resource integration, including the incorporation of Pillar 2 into the team. In addition, integrating participants from Pillar 4 (IARC Handbooks, WHO Classiciation of Tumours) may also be beneficial.

Key publications

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- Benitez Fuentes JD, Morgan E, de Luna Aguilar A, Mafra A, Shah R, Giusti F, Vignat J, Znaor A, Musetti C, Yip CH, Van Eycken L, Jedy-Agba E, Piñeros M, Soerjomataram I. Global Stage Distribution of Breast Cancer at Diagnosis: A Systematic Review and Meta-Analysis. JAMA Oncol. 2024 Jan 1;10(1):71-78. PMID: 37943547; PMCID: PMC10636649.
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References

- Web page of the GBCI Team
- Web site of the WHO Global Breast Cancer initiative

Oesophageal Cancer (ECA) Team

Cancer types Teams
➔ Starting date: June 2022

Members

Team leaders: Dr Valerie McCormack (Deputy Branch Head, ENV) and Dr Behnoush Abedi-Ardekani (Scientist, GEM).

Team members: The Team comprises 16 members, including 11 scientists, 5 postdoctoral scientists, and 1 doctoral student. It relies on a multi-Branch organization, with 2 members in CSU (Pillar 1), 4 members in GEM and 1 member in NME (Pillar 2), 5 members in EGM, 4 members in ENV, and 1 member in EPR (Pillar 3). The Team plans to integrate one scientist working in the IARC Monographs programme in the ESC Branch (Pillar 4).

➔ Dr Eileen Morgan (Postdoctoral Scientist, CSU); Dr Melina Arnold (Scientist, CSU); Dr Mahdi Sheikh (Scientist, GEM); Dr Sergey Senkin (Postdoctoral Scientist, GEM); Dr Paul Brennan (Branch Head, GEM); Dr Pekka Keski-Rahkonen (Scientist, NME); Dr Fazlur Talukdar (Postdoctoral Scientist, EGM); Dr Zdenko Herceg (Branch Head, EGM); Dr Jiri Zavadil (Deputy Branch Head, EGM); Dr Tarik Gheit (Scientist, EGM); Ms Zhiyuan Fan (Doctoral Student, EGM); Dr Hannah Simba (Postdoctoral Scientist, ENV); Dr Joachim Schüz (Branch Head, ENV); Dr Clement Narh (Visiting Scientist, ENV); Dr Melitah Motlhale (Postdoctoral Scientist, ENV); Dr Tarik Gheit (Scientist, EPR).

The ECA Team has an open membership policy. All IARC Branches with scientists working on oesophageal cancer are welcome to join.

Objectives

Oesophageal cancer is categorized into two main histological types: about 80% is oesophageal squamous cell carcinoma (ESCC), and about 20% is adenocarcinoma, based on global incidence data. However, significant regional variations exist in these statistics. The risk factors associated with oesophageal cancer are multifactorial and vary by histological type.
These include:

- **Established risk factors**: alcohol consumption, tobacco use, and radiation exposure.
- **Likely risk factors**: consumption of hot beverages and indoor air pollution from polycyclic aromatic hydrocarbons (PAHs).
- **Uncertain risk factors**: factors such as HIV, mycotoxins, nitrosamines, and pickled foods.

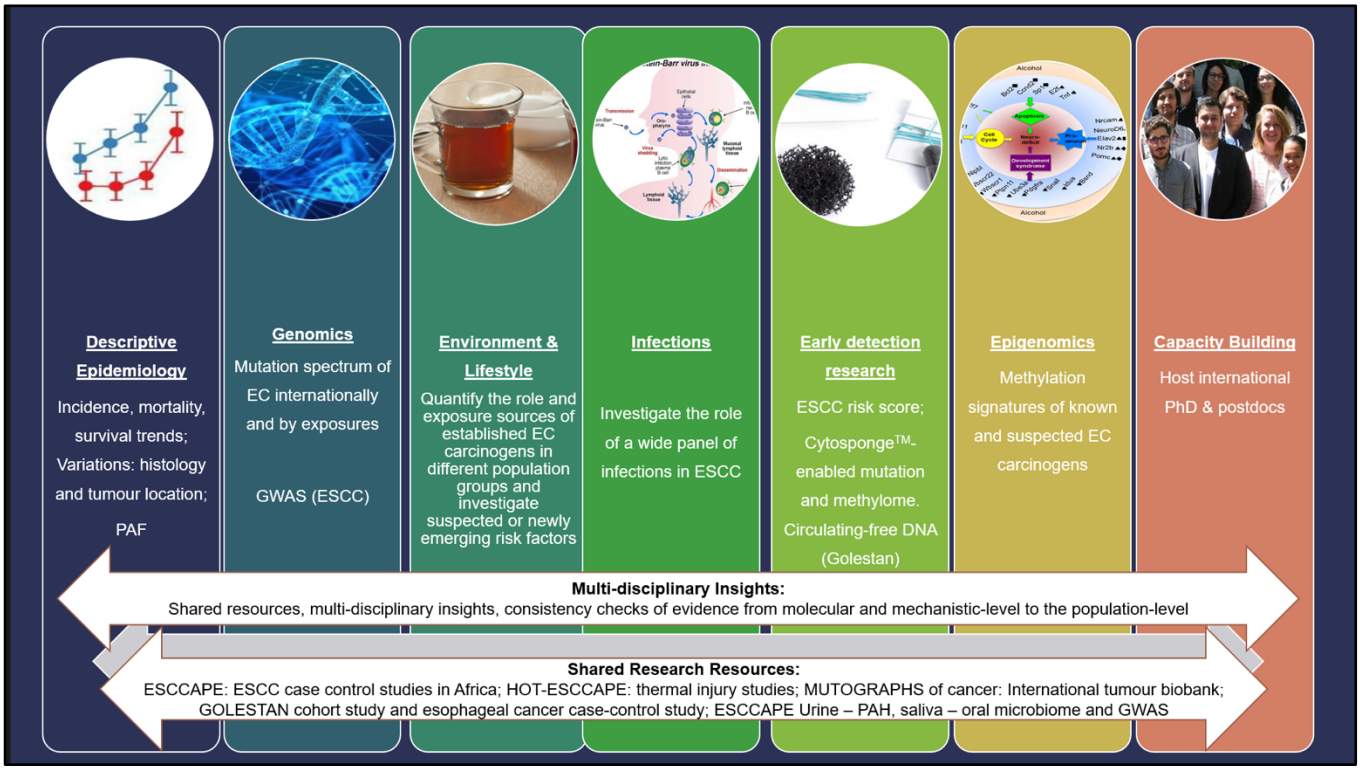
The highest incidence rates of ESCC are found in Asia and Africa, although the reasons for these localized geographical patterns remain poorly understood. Oesophageal cancer is characterized by a dismal prognosis, with median survival ranging from 6 to 18 months in LMICs.

Research focus

The primary aim of the ECA Team is to enhance research on the prevention and early detection of oesophageal cancer, particularly ESCC, on a global scale. This cross-Agency research approach seeks to leverage data sharing, resource pooling, and multidisciplinary perspectives that span from mechanistic insights to population-level implications.

Before the formal establishment of the ECA Team, many inter-Branch collaborations focused on oesophageal cancer already existed. The ECA Team consolidates these efforts, facilitating meetings to strengthen current collaborations and identify new opportunities. The objectives of the ECA Team include:

1. **Descriptive epidemiology**: To analyse incidence patterns and time trends of oesophageal cancer worldwide (CSU, GEM, ENV).
2. **Novel risk factor identification**: To explore and identify new risk factors for oesophageal cancer across diverse populations using traditional, molecular, and genetic epidemiological methods (GEM, ENV, EGM, EPR, NME).
3. **Early detection strategies**: To develop feasible early detection strategies for oesophageal cancer in various populations, using traditional, molecular, and genetic epidemiology (GEM, ENV, EPR, EGM).



Workplan progress

Projects and consortia

The ECA Team's scientific activities are supported by several major consortia, including:

- **ESCCAPE**: The Oesophageal Squamous Cell Carcinoma African Prevention Research (ESCCAPE) consortium is a collaborative effort aimed at investigating the etiological epidemiology of squamous cell carcinoma in Africa. The goal is to inform future primary prevention strategies by conducting studies that shed light on the causes of oesophageal cancer, particularly ESCC. ESCCAPE includes case–control studies from Kenya, Malawi, and the United Republic of Tanzania, entailing more than 1300 cases and 1300 controls.

- **ENDOSCCAPE**: This proposal for an endoscopy survey involves scientists from three Branches (ENV, GEM, NME) and focuses on Malawian adults aged 50–70 years (N = 400 asymptomatic community members). The programme includes Lugol's chromoendoscopy, capsule-sponge technologies, as well as urine and blood samples, questionnaires, and nitrosamines analysis.

- **Mutographs**: This multicentre international study collected thousands of cancer and non-tumoural tissue samples between 2017 and 2023, including 1500 oesophageal cancers and nearly 1000 non-tumoural tissues across both histological types. The aim is to discover and analyse mutational signatures caused by environmental exposures. Analysis of 500 ESCC samples from eight countries with varying incidence rates revealed no significant differences between the countries.

- **PROMINENT**: This major project investigates clonal expansion in normal tissues that may lead to cancer. It is based on the Mutographs biorepository and includes both types of oesophageal cancer in its scope. The research on squamous cell carcinoma is conducted in collaboration with the Sanger Institute. The Team is also actively involved in the African Esophageal Cancer Consortium.

- The Team is highly active in the **African Esophageal Cancer Consortium (AfrECC)**.

Since its inception in mid-2022, the ECA Team has implemented its workplan, leading to several projects and results, including:

- **Descriptive epidemiology and case–control study insights**:
  - ➔ An international study on anatomical tumour location in ESCC, examining determinants by sex and ESCC risk factors (CSU, ENV, GEM). Analyses have been completed.

- **ESCCAPE**:
  - ➔ Case–control studies in East Africa focusing on the role of smokeless and smoking tobacco in ESCC. Notable publications include findings by Simba (IJC) and an expansion to the Johannesburg Cancer Study (Motlhale, submitted).
  - ➔ Draft completed for the ESCC risk score in Africa (ENV), with discussions ongoing regarding Malawi's inclusion.

- **Epigenomics**:
  - ➔ Testing DNA methylation and molecular markers of ESCC in minimally invasive biospecimens for early detection (EGM, ENV).
  - ➔ Addressing low DNA yields from cytosponges by planning to collect another set and modify the analytical process.
  - ➔ Investigating infections associated with ESCC (ENV, EGM): The first analytical phase has been completed, identifying some infections (e.g. cytomegaloviruses), with expansion plans under way.

- **Genomic studies**:
  - ➔ Investigating the mutation spectrum in ESCC, focusing on variations by sex and exposure.

- **Networking and communication**:
  - ➔ Integrating IARC's activities with other international efforts, including AfrECC. This collaboration has been achieved, and grants have been submitted.
  - ➔ Linking EC-wide activities across IARC to a single integrated website to showcase the broader programme. The ESCCAPE website is actively maintained and updated.

Governance

The members of the ECA Team have convened as a whole in-person once to date and have established a schedule for triannual meetings in January, May, and September. These meetings are designed to provide an overview of the Team's activities. In addition to these formal gatherings, the ECA Team members hold research meetings focused on specific tasks, such as implementing programmes and preparing grant applications.
The co-leaders of the Team view the ECA Team as a platform for exchange and interaction, operating as an informal governance structure that promotes collaboration among members.

Links with WHO
The co-leaders of the Team have initiated preliminary contacts with WHO headquarters (specifically with Dr Jérôme Salomon); however, no formal collaboration on oesophageal cancer has yet been established with WHO. The ECA Team aims to investigate the poorly understood geographical distribution of oesophageal cancer worldwide. Until this knowledge is acquired, there are currently no health policy implications for WHO. In regions where tobacco and alcohol are significant contributors, WHO already has relevant action plans in place.

Applications and Grants

Key funding sources: The primary funders of the ECA Team's projects include the World Cancer Research Fund (WCRF), Cancer Research UK Grand Challenges (CRUK), and the United Kingdom Medical Research Council (MRC). The ECA Team is also exploring new funding opportunities in areas of interest such as risk factors in young populations, biomass fuels, and oral health and hygiene. However, it is important to note that funding for ECA initiatives remains low at the global level, making it challenging to secure additional resources. Two ENV-NME-GEM joint applications have been submitted since the ECA Team was started.

Publications

See "Key publications" below.

Training

The co-leaders of the CCG Team have reported a significant number of postdoctoral scientists within the ECA Team, as well as involvement in the BIG CAT NCI award (Beginning Investigator Grant for Catalytic Research).

Key collaborations

Cooperation across IARC Branches

The main contributors to the ECA Team are GEM, EGM, CSU, and ENV. CSU leads on descriptive epidemiology. ENV leads many of the African studies, including a large fieldwork component. GEM and EGM lead on their respective expertise in genomics and epigenomics, with stand-alone studies and, where possible, research embedded within ENV and CSU fieldwork studies.

Collaboration with external partners

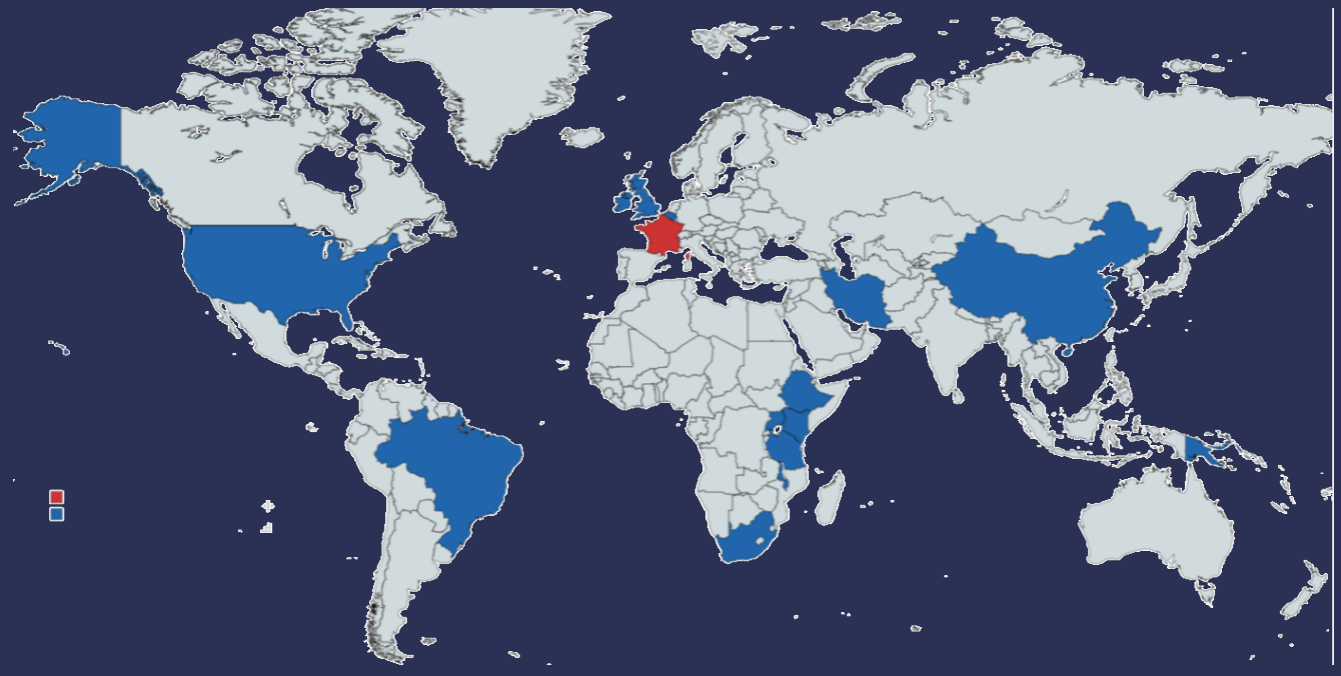
The ECA Team collaborates with partners across 19 countries worldwide, including:

- Africa: Zimbabwe, Zambia, Kenya, Ethiopia, Botswana, Ghana, Morocco, Malawi, United Republic of Tanzania
- Asia: Islamic Republic of Iran, Russian Federation, India, China
- America: Brazil, USA
- Europe: Czechia, Croatia, Germany, Ireland, United Kingdom, France, Finland

This international collaboration is illustrated in the map below.

Key scientific partners include:

- African Esophageal Cancer Consortium (AfrECC): comprising 90 members, with Dr Valerie McCormack serving on the Steering Committee.
- Moi University in Kenya
- Kilimanjaro Clinical Research Institute in the United Republic of Tanzania
- Kamuzu University of Health Sciences in Malawi
- Cambridge University, Imperial College, and Queen's University in the United Kingdom
- Ghent University in Belgium
- University of California, San Francisco
- National Cancer Institute (NCI) in the USA
- National Cancer Institute (INCA) in Brazil



Main innovations

According to the co-leaders of the Research Team, the primary innovations of the ECA Team include:

- **Focus on an understudied cancer**
- **International dimension**: Collaborating across regions, including Asia, Africa, Europe, and South America, with a strong emphasis on LMICs.
- The **sharing of biospecimens**
- The promotion of **appropriate health technology**

Contributions to MTS implementation

The activities of the ECA Team align with IARC's vision, mission, and priorities as outlined in the MTS 2021–2025, which aims to identify the causes of cancer and produce evidence-based science for global cancer control and prevention. The Team exemplifies cross-branch collaboration, engaging with scientists from the GEM, EGM, CSU, and ENV Branches.

Fundamental priorities
The workplan of the ECA Team corresponds with the MTS 2021–2025 priorities, specifically focusing on the first three fundamental priorities:

- ➔ **Describing cancer occurrence**: Conducting descriptive epidemiology on oesophageal cancer.
- ➔ **Understanding cancer causes**: Implementing programmes in genomic and epigenomic research.
- ➔ **Evaluating cancer prevention interventions**: Engaging in extensive fieldwork as part of African studies.

Main challenges

The ECA Team faces several challenges, including:

- **Limited research focus**: Oesophageal cancer is under-researched globally and is often considered a "poor person's cancer", which is not prioritized in funding by HICs. As a result, ECA Team members must target generic calls for applications rather than specific ones for oesophageal cancer.
- **Climate change considerations**: The team should integrate the "climate change agenda" concerning clean cooking fuels and water sources into their research.
- **IARC's role**: There is a pressing need for IARC to mobilize international efforts to address this neglected cancer, given its early onset, poor prognosis, and localized burdens. WHO cannot implement targeted actions until preventive or early detection strategies are established. According to the Team co-leaders, IARC should continue to promote research in this area, which requires investment in expertise and human resources.

Next steps

The co-leaders of the ECA Team have identified the following next steps for the Team's development:

- ➔ **Descriptive research**: Continue efforts related to CI5-XII and GLOBOCAN data.
- ➔ **Aetiology studies**: Focus on AfrECC, which will include initiation of an African ESCC Pooling Project, with IARC leading the data coordinating centre.
- ➔ **Comparative analyses**: Examine results from Golestan, China, and African hotspots.

- ➔ **Molecular changes**: Compare molecular alterations in non-tumoural oesophageal tissues from regions with stark differences in incidence rates.
- ➔ **Early detection techniques**: Explore the use of endoscopy or capsule sponge technologies for early detection and etiology, potentially incorporating AI technologies.
- ➔ **Health technology development**: Promote the adoption of appropriate health technologies.

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RECOMMENDATIONS

The ECA Team aims to advance global research on the prevention and early detection of oesophageal cancer, a significant cause of cancer-related mortality worldwide. This focus offers a vital opportunity for IARC to impact prevention strategies and foster new collaborations, both internally and externally.

- ✓ In the short term, the ECA Team is encouraged to strengthen its governance within the IARC structure. This includes organizing Agency-level coordination meetings (currently held only once every two years), specifying its scientific strategy, and clearly defining priorities.
- ✓ In the medium term, ECA Team members have suggested exploring new fields of investigation, such as climate change and health inequities, while seeking additional funding opportunities, including direct funding avenues (e.g. WHO Regional office for Africa, Agence Française de Développement).

Key publications

- Middleton DRS, Mmbaga BT, Menya D, Dzamalala C, Nyakunga-Maro G, Finch P, et al.; ESCCAPE (2022). Alcohol consumption and oesophageal squamous cell cancer risk in east Africa: findings from the large multicentre ESCCAPE case-control study in Kenya, Tanzania, and Malawi. Lancet Glob Health. 10(2):e236– 45. PMID:34921758
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- Talukdar FR, Soares Lima SC, Khoueiry R, Laskar RS, Cuenin C, Sorroche BP, et al. (2021). Genome-wide DNA methylation profiling of oesophageal squamous cell carcinoma from global high-incidence regions identifies crucial genes and potential cancer markers. Cancer Res. 81(10):2612–24. PMID:33741694
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- Sheikh M, Poustchi H, Pourshams A, Khoshnia M, Gharavi A, Zahedi M, et al. (2020). Household fuel use and the risk of gastrointestinal cancers: the Golestan Cohort Study. Environ Health Perspect. 128(6):67002. PMID:32609005

References

- Webpage of the ECA Team
- Website of the ESCCAPE programme

Oral Cancer Team (OCT)

Cancer types Teams
➔ Starting date: September 2023

Members

Team leaders: : Dr Shama Virani (Scientist, GEM), Dr Andre Carvalho (Deputy Branch Head, EPR), Béatrice Lauby-Secretan (Head, IARC Handbooks of Cancer Prevention programme, ESC), Harriet Rumgay (Scientist, CSU). Team Leaders have expertise across the OCT Team themes with one co-leader per Pillar.

Team members: The OCT Team comprises of 13 Team members from IARC, including 2 members in the CSU Branch (Pillar 1), 6 members in the GEM Branch (Pillar 2), 2 members in the EGM Branch, 1 member in the EPR Branch (Pillar 3), and 2 members in the ESC Branch (Pillar 4).

- ➔ Dr Amanda Ramos da Cunha (Postdoctoral Scientist, CSU); Dr Carol De Carvalho (Scientist, GEM); Ms Elmira Ebrahimi (Doctoral Student, GEM); Dr Sandra Perdomo (Scientist, GEM); Dr Apiwat Sangphukieo (Postdoctoral Scientist, GEM); Dr Mahdi Sheikh (Scientist, GEM); Dr Tarik Gheit (Scientist, EGM); Dr Jiri Zavadil (Deputy Branch Head, EGM); Dr Suzanne T. Nethan (Visiting Scientist, ESC)
- ➔ External members: Dr David I. Conway (University of Glasgow, United Kingdom); Dr Tom Dudding (University of Bristol, United Kingdom); Dr Irena Duś-Ilnicka (Wroclaw Medical University, Poland); Dr Olena Mandrik (University of Sheffield, United Kingdom); Dr Gamege Ranasinghe (Ministry of Health, Sri Lanka); Dr Alan Roger dos Santos Silva (State University of Campinas, Brazil); Dr Pierre Saintigny (Centre Léon Bérard and Université Claude Bernard Lyon 1, France); Dr Pichit Sittitrai (Chiang Mai University, Thailand); Dr Benoit Varenne (WHO headquarters); Dr Saman Warnakulasuriya (King's College London, United Kingdom)

Objectives

Context

Oral cancer ranks as the 16th most common cancer worldwide in terms of incidence and mortality. The primary risk factors include:

- ➔ Consumption of tobacco in all forms (both smoked and smokeless)
- ➔ Consumption of alcoholic beverages
- ➔ Consumption of areca nut (including betel quid)

Oral cancer is a leading cause of death in regions where smokeless tobacco and/or areca nut usage is prevalent. Despite its significance, oral cancer prevention remains largely under-researched. Traditional epidemiological approaches have laid the groundwork for understanding the risk factors, populations, and behaviours associated with oral cancer. However, progress in this field has been slow due to a lack of clear pathways for advancing research.

In 2021, the *IARC Handbooks* programme conducted a comprehensive review of the effectiveness of primary and secondary interventions for oral cancer prevention (Volume 19). After this review, several supplemental projects were planned to address topics related to oral cancer prevention. Recognizing the need for coordination in this area, the OCT Team was officially established in September 2023 to streamline efforts and leverage external expertise.

Research focus

The primary ambition of the OCT Team is to foster innovative and collaborative research across multidisciplinary themes through cross-agency and international partnerships, with a particular focus on LMICs. The overarching goal is to generate evidence that can effectively reduce the global burden of oral cancer.

The scientific activities of the OCT Team are organized around several key themes that directly contribute to the prevention of oral cancer worldwide:

- **Surveillance:** Evaluate population-specific trends related to oral cancer incidence, survival rates, exposure factors, and demographics.

- **Primary prevention:** Develop studies aimed at promoting the cessation of smoking, alcohol consumption, and smokeless tobacco use.
- **Early detection:** Create tools and approaches designed to achieve downward stage shifts in oral cancers and validate these methods for global use.
- **Population-based epidemiology:** Identify biological and population-specific factors associated with oral cancer incidence and prognosis across diverse populations.
- **Knowledge mobilization:** Synthesize evidence to inform stakeholders, clinicians, community health workers, policymakers, and scientists.

Governance

The OCT Team is co-led by four scientists, each representing one of the four Pillars of IARC. Dr Harriet Rumgay oversees the administrative and logistical aspects of the Research Team. The leadership team meets regularly to discuss strategy, set goals, determine scientific direction, and plan scientific meetings.

Links with WHO
The OCT Team includes a representative from WHO headquarters, Dr Benoit Varenne, who is the Dental Officer and leads the Oral Health Unit. There has been strong collaboration between the OCT Team and WHO headquarters, particularly during the launch of *IARC Handbook* sVolume 19 on oral cancer prevention.

To achieve these objectives, the OCT Team emphasizes cross-Branch collaboration, bringing together members from various Branches to identify important research areas that are well-suited for multidisciplinary approaches. By fostering innovative ideas through increased interaction among internal and external scientists, the OCT Team aims to unite scientific partners who recognize the significance of this area and are eager to collaborate with IARC on oral cancer initiatives. The focus on oral cancer, particularly in LMICs, aligns directly with IARC's mission to reduce the cancer burden globally.

Workplan progress

Projects and consortia

The workplan of the OCT Team addresses scientific challenges related to cancer surveillance, primary prevention, early detection, population-based epidemiology, and knowledge mobilization through structured scientific discussions. Research meetings are held every 12 weeks, focusing on specific themes such as genomics and screening, and guests are welcome to attend if the topic is of interest. Team members, both internal and external, can choose to develop projects as outcomes of these meetings. To facilitate discussion and information sharing, the OCT Team has established a dedicated channel on Teams and formed working groups based on specific scientific interests.

The programme of work for the OCT Team encompasses the following topics and projects:

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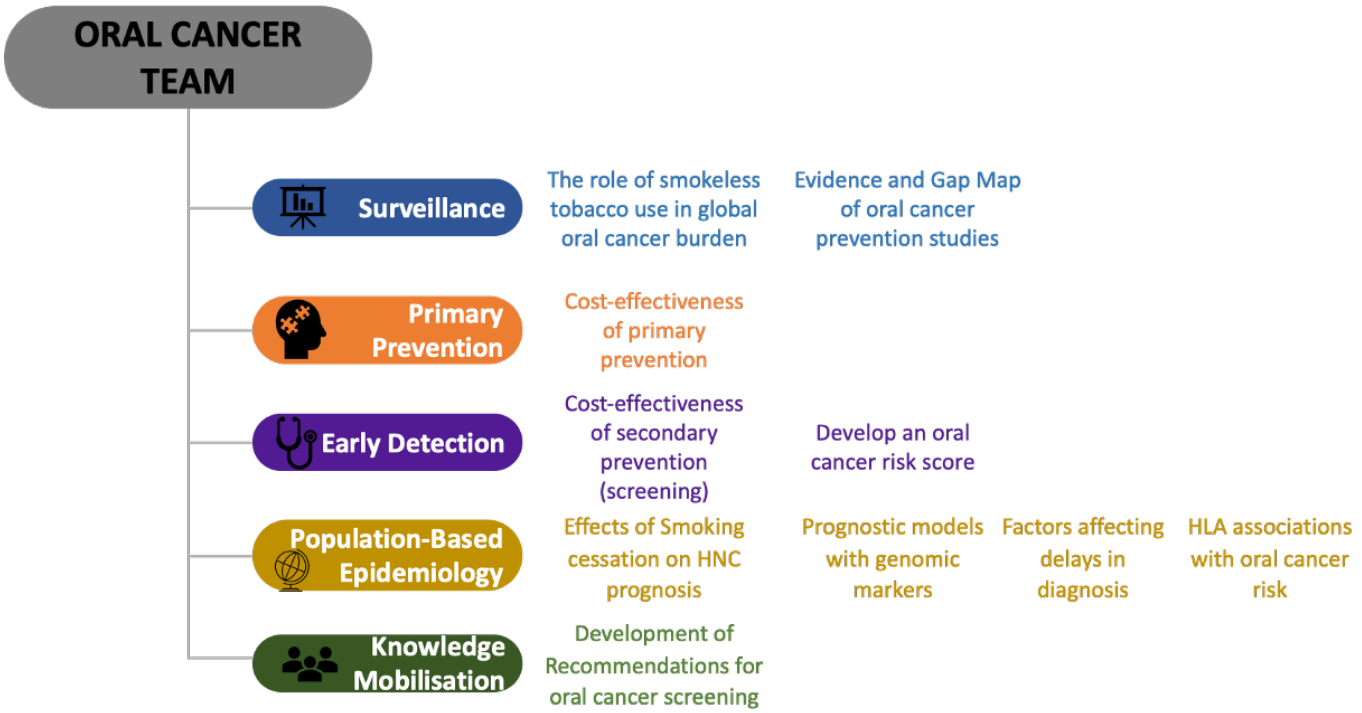


➔ **Surveillance**

- **Title**: The Role of Smokeless Tobacco and Areca Nut in Global Oral Cancer Burden (PAF-SLT/AN)
  Aim: Estimate the impact of smokeless tobacco and areca nut use on oral cancer incidence, specifically in South Asia and the Western Pacific, where prevalence is highest.
- **Title**: Evidence and Gap Map on Oral Cancer Prevention
  Aim: Develop a visual interactive display of the available evidence and identify gaps in the literature on primary and secondary prevention of oral cancer using a systematic approach.

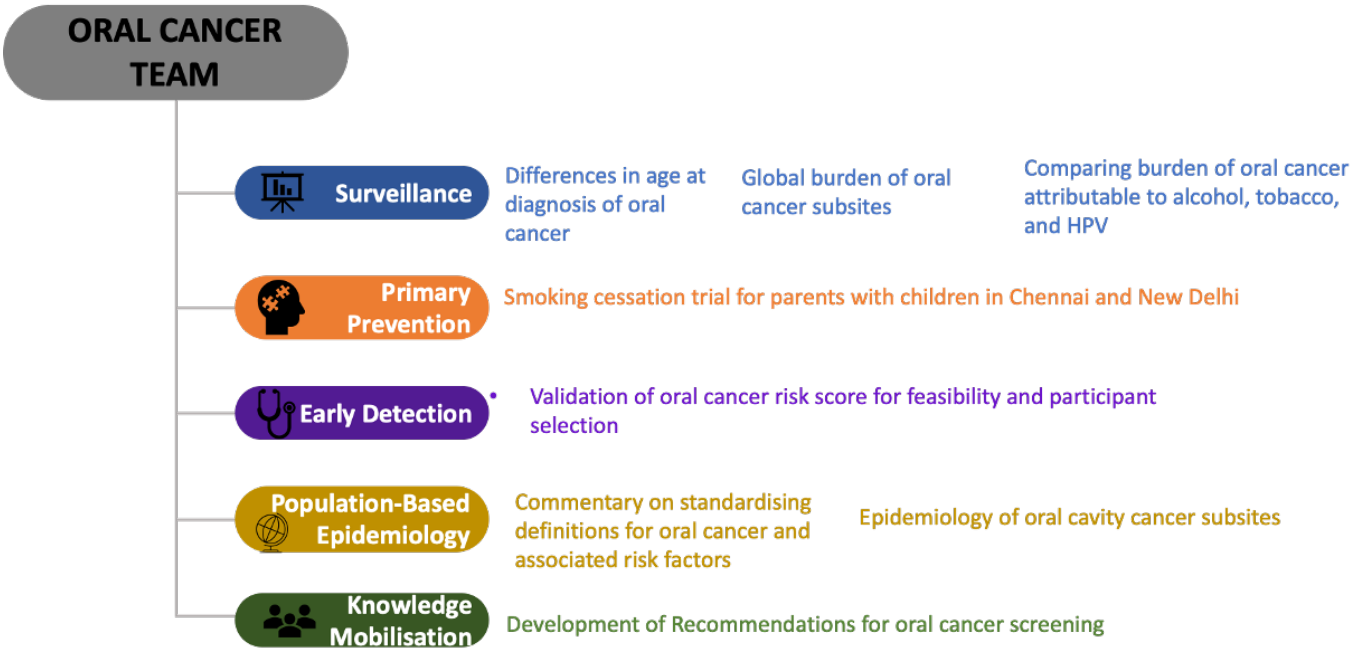
➔ **Primary prevention**

- **Title**: Cost-Effectiveness Analyses of Interventions for Oral Cancer Prevention
  Aim: Assess the cost-effectiveness of primary interventions as "best buy" strategies for oral cancer prevention, including behavioural interventions for the cessation of smokeless tobacco and areca nut use.

➔ **Early detection**

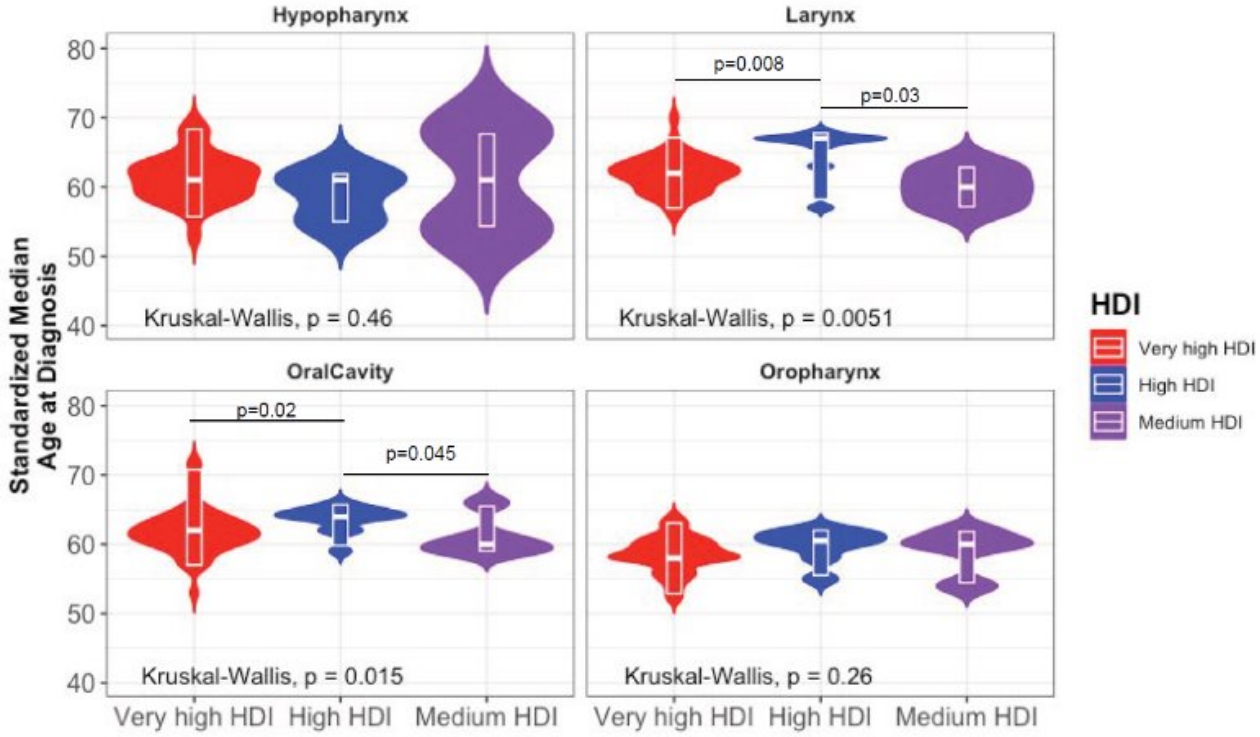
- **Title**: Strategies for Oral Cancer Early Detection
  Aim: Assess the strategies and feasibility of implementing early detection programmes for oral cancer.

The programme of work of the OCT Team also includes several emerging projects, on the following topics:



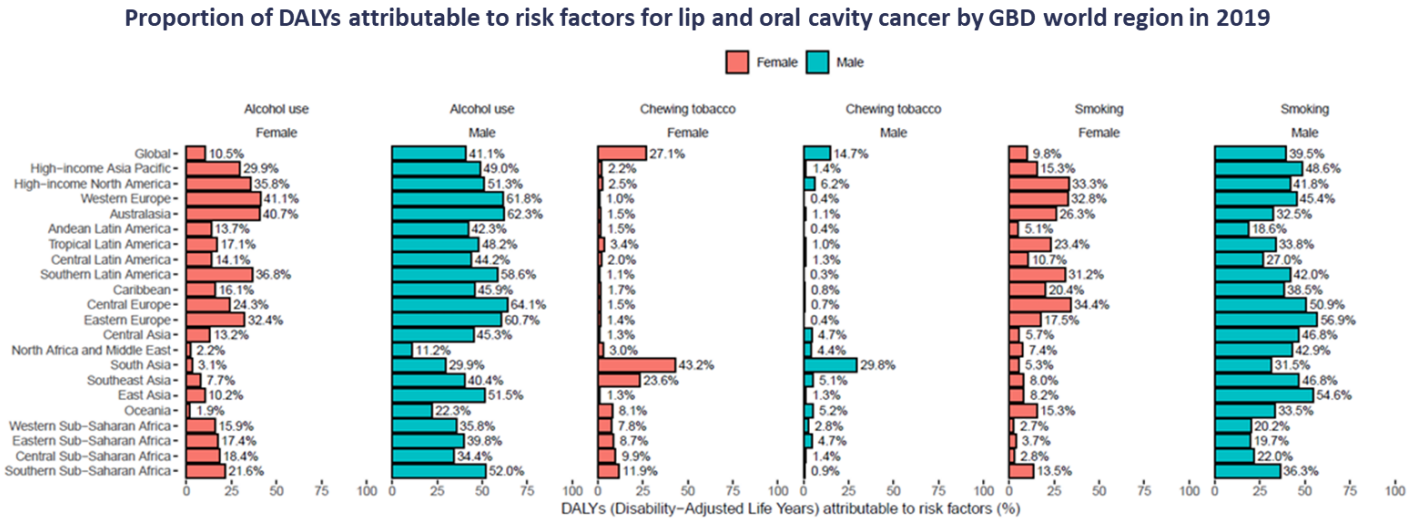
➔ **Surveillance**

- **Title**: Differences in Age at Diagnosis of Oral Cancer
  Aim: To compare median age at diagnosis of oral cancer subsites across populations
  Median age at diagnosis of oral cancer subsites among women by Human Development Index group



Source: Source: Virani and Rumgay, in preparation

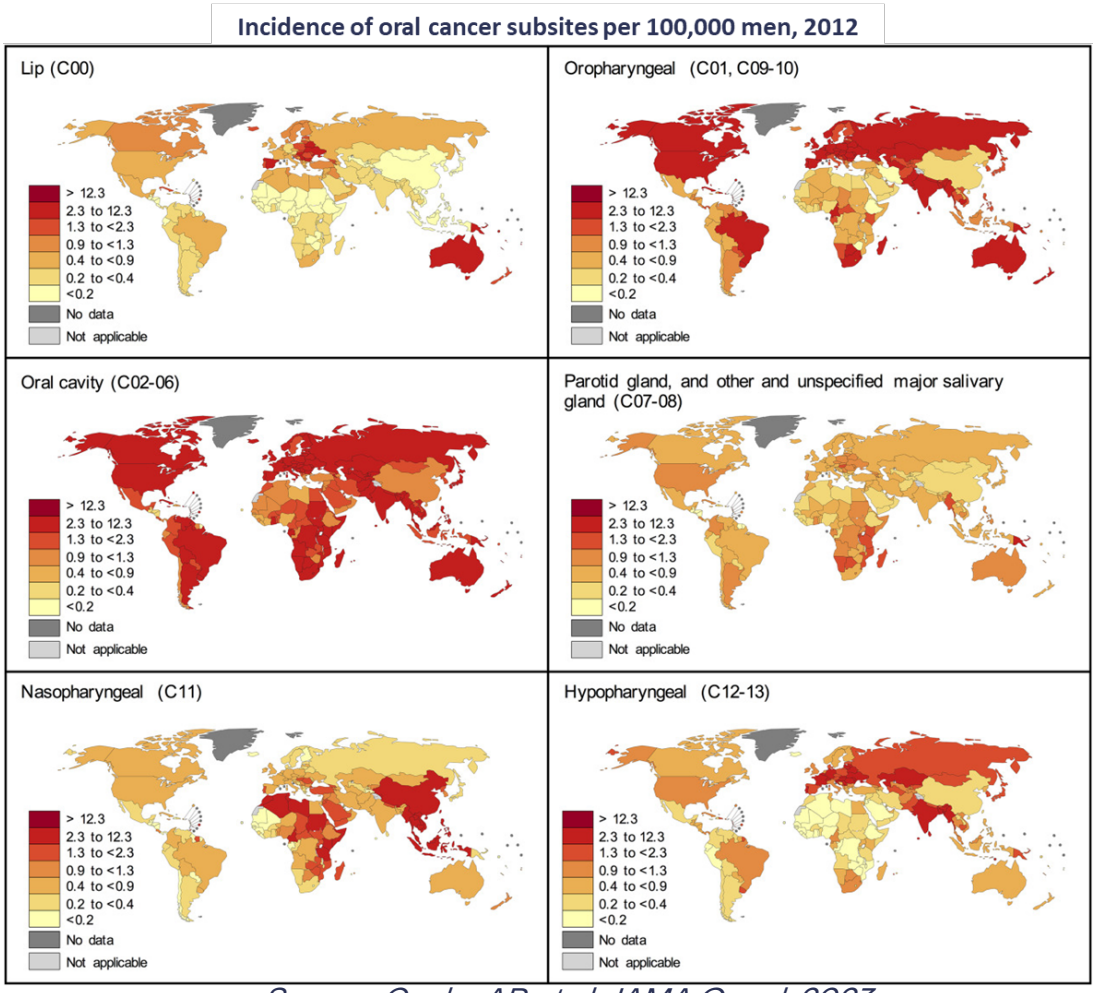
- **Title**: Global Burden of Oral Cancer Subsites
  Aim: To estimate the global and national burden of specific oral cancer subsites/



Source: Shield et al. CA A Cancer J Clinicians, 2016

➔ **Early detection**

- **Title**: Development of a Risk-Stratified Score for Oral Cancer Screening
  Aim: Work on a risk score to identify high-risk populations for early detection of oral cancer.



Source: Cunha AR et al. JAMA Oncol, 2023

➔ **Population-based epidemiology**

- Commentary on Standardizing Definitions for Oral Cancer and Associated Risk Factors
  Aim: Clarify the use of oral cancer terminology to prevent misclassification of exposures, such as HPV infection, to subsites where they are not causal (e.g., oral cavity vs. oropharynx instead of 'oral cancer').
- Epidemiology of Oral Cavity Cancer Subsites
  Aim: Evaluate the patient population and prognostic profiles of patients with oral cavity cancer, stratified by their specific anatomical location. There is emerging evidence that the location of oral cavity cancers has been shifting over the past decade.

Applications and grants

Given the recent establishment of the IARC OCT Team, there have been no funding applications yet. However, team members are currently involved in several projects funded by the Institut National du Cancer in France and the European Commission. The OCT Team members have submitted applications and identified several targets for future grant applications, including:

– Virani (IARC), Saintigny (CLB): Prognostic determinants of tumour immune microenvironment (INCa).

– Conway (UK): HEADSpAcE CHALLENGE (UKRI).

– Conway (UK), Perdomo (IARC), Silva (Brazil): Elucidating the mutational signatures of biological and environmental causes of oral potentially malignant disorders (OPMDs) (Moonrise, US NCI).

Publications

Given the recency of the OCT Team, there have been no publications directly issued from the team. “Key publications” below presents the publications of the different Branches that are pertinent to the Team.

Training

The co-leaders of the OCT Team have not reported any training activities since the establishment of the Team. However, several Visiting Scientists have been involved in related projects with OCT Team members:

- **Dr Delfin Francis**: Awardee of the IARC Mid-Career Scientist Fellowship
  Project: Clinical Trial on Smoking Cessation Intervention Strategy, measuring urinary cotinine levels in children of parents who smoke.
- **Dr Devaraja Kariyanna**: Awardee of the UICC Fellowship
  Project: Multicenter trial to validate a pre-screening risk stratification tool for identifying high-risk individuals for oral cancer.

Key collaborations

Cooperation across IARC Branches
The governance structure and workplan of the OCT Team facilitate collaboration across all IARC Pillars, engaging multiple Branches including CSU, GEM, EGM, EPR, and ESC.

Collaboration with external partners
The OCT Team comprises members from several partner institutions, including:

- **UK:** University of Glasgow; University of Bristol; University of Sheffield; King's College London
- **France**: Centre Léon Bérard; Université Claude Bernard Lyon 1
- **Poland:** Wroclaw Medical University
- **Sri Lanka:** Ministry of Health
- **Thailand:** Chiang Mai University
- **Brazil:** State University of Campinas

The OCT Team coordinates the HEADSpAcE consortium, which aims to investigate the various reasons behind the poor prognosis of head and neck cancers. This includes examining individual and structural factors contributing to late diagnosis, as well as the influence of lifestyle, infectious agents, and genetic factors on outcomes, alongside adherence to clinical guidelines in various settings. Initiated in 2019, this Translational Studies of Head and Neck Cancer in South America and Europe (HEADSpAcE) project is funded by the European Union (grant no. 825771) and brings together 15 partner institutions with a strong history of collaboration in the study of head and neck cancers. Thanks to the HEADSpAcE consortium, IARC now hosts a significant number of samples in its biorepository and has developed a harmonized database for oral cancer, encompassing data from 12,000 to 15,000 patients.

Main innovations

As part of its emerging projects, the OCT Team aims to develop a risk score for oral cancer as an early detection strategy, specifically targeting high-risk populations for screening. Several surveillance studies are currently under-way to evaluate the burden of oral cancer associated with specific exposures.

Contributions to MTS implementation

Fundamental priorities

The workplan of the OCT Team aligns perfectly with the priorities outlined in the IARC MTS 2021-2025, contributing to the four fundamental priorities:

- **Describing the occurrence of cancer**: Projects focusing on the global oral cancer burden and the population impact of smokeless tobacco and areca nut use on oral cancer.
- **Understanding the causes of cancer**: Research on genomic markers, HLA associations with oral cancer risk, and the effects of smoking cessation.
- **Evaluating cancer prevention interventions**: Projects assessing the cost-effectiveness of primary and secondary prevention interventions and the development of an oral cancer risk score.
- **Synthesizing and mobilizing knowledge**: Strengthening global capacities in cancer science, exemplified by the publication of *IARC Handbooks* Volume 19 on Oral Cancer Prevention.

Main challenges

The OCT Team faces several key challenges:

- **Time and resources**: There is a lack of administrative support, with scientists currently managing administrative duties rather than focusing on scientific work. The OCT Team suggests using LY2 or LY3 positions for administrative needs or establishing administrative internships.

- **Management of new external Team members**: The Team receives frequent requests to join, necessitating the definition of criteria for core members. The OCT Team seeks administrative guidance on the selection process.
- **Balancing responsibilities**: The co-leaders acknowledge the importance of promoting leadership among early to mid-career scientists and request greater recognition of Team activities in the ePMDS.

Next steps

According to the co-leaders of the OCT Team, the following steps will be taken for the development of the Team:

- ➔ **Implement the work programme:** Actively promote new activities aligned with the objectives of the OCT Team.
- ➔ **Apply for funding:** Seek resources for new initiatives through ongoing applications with organizations such as INCa, CRUK, and US NCI.
- ➔ **Promote grant applications:** Encourage team members to submit grant applications and facilitate the sharing of publications and research plans in a standardized manner.
- ➔ **Interact with World Code Against Cancer (WCAC) programmes:** Collaborate with the programmes on the WCAC across Europe, Asia, and Latin America.
- ➔ **Engage with WHO regional offices:** Strengthen interactions to share data and insights effectively.

RECOMMENDATIONS

Established in September 2023 after the publication of the IARC Handbooks volume on Oral Cancer Prevention, the OCT Team has already achieved significant initial publications. It is well structured, with co-leaders from each of the four Pillars and representation from WHO headquarters. The team benefits from a large network of international scientific partners, including the HEADSpAcE consortium, making its activities promising.

- ✓ The OCT Team should consider producing a supplementary document to Handbooks Volume 19, such as a matrix analysis of 200 studies on oral cancer, in close collaboration with WHO headquarters.
- ✓ The OCT Team should define effective strategies to reinforce collaborations with WHO regional offices and clearly outline its contributions and interactions with the programmes related to the Codes Against Cancer.

Key publications

- IARC (2023). Oral cancer prevention. IARC Handb Cancer Prev. 19:1–358.
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References

- Webpage of the OCT Team
- IARC Handbook on oral cancer prevention
- Webpage of the HEADSpAcE Consortium

2

Assessment : Innovations Teams

Biostatistics and Data Integration (BDI) Team

Members

Team leaders: Dr Vivian Viallon (Scientist NME) and Dr Pietro Ferrari (Branch Head, NME)

14 team members from one Branch, NME, Pillars 2. One ECVS and one admininistrative assistant should be recruited:

- Dr Heinz Freisling (Scientist, NME); Ms Carine Biessy (Research Assistant, NME); Mr Bertrand Hemon (Research Assistant, NME); Ms Karina Zaluski (Admin Assistant, NME); 1 administrative assistant to be recruited; Dr Marie Breeur (ECVS, NME); Dr Niki Dimou (ECVS, NME); Dr Ali Farnudi (ECVS, NME); Mr Quan Gan (ECVS, NME); Dr Komodo Matta (ECVS, NME); Ms Fanélie Vasson (ECVS, NME); Ms Diana Wu (ECVS, NME); Dr Yue Zhai (ECVS, NME).

Innovations Teams
➔ Starting date: January 2021

Objectives

The primary aim of the BDI Team is to **investigate the role of nutritional exposures, the exposome, and metabolic disruptions in cancer development.** This will be achieved through the development of advanced statistical tools.

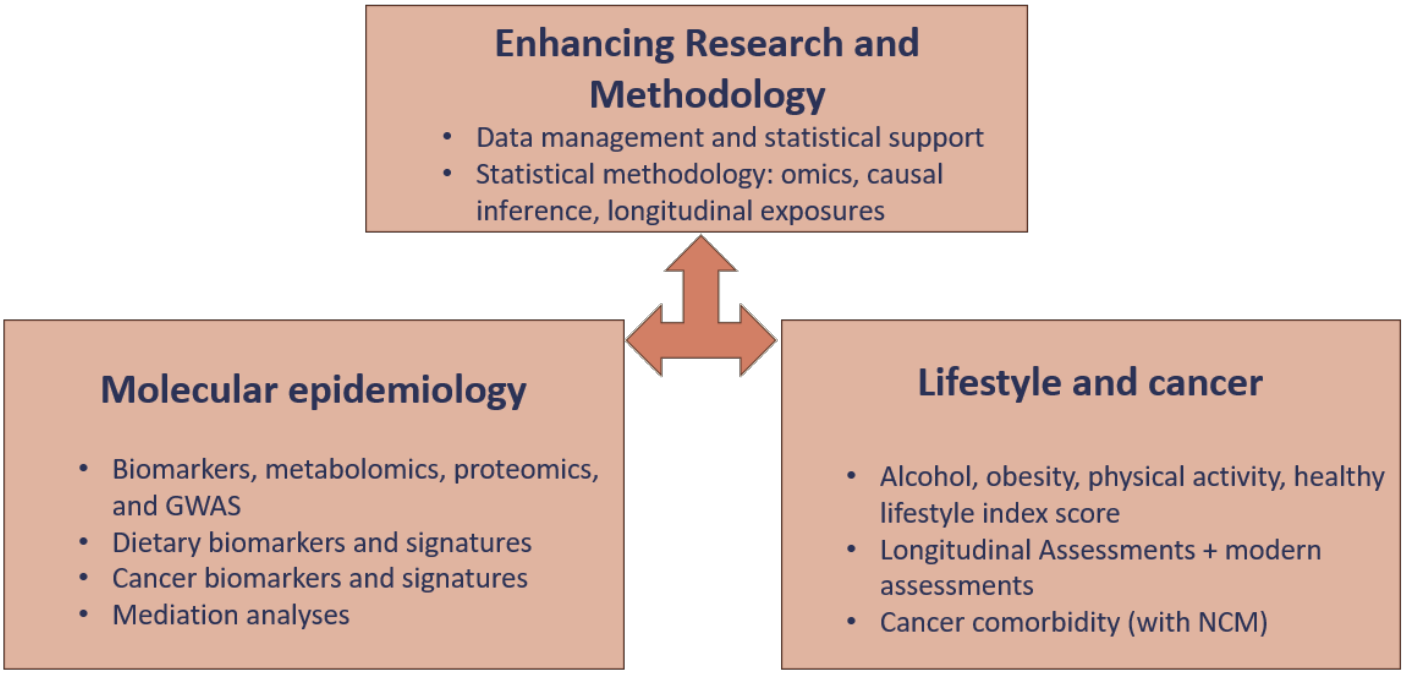
Research focus

With the increasing wealth of data derived from large prospective studies (such as GWAS, metabolomics, and proteomics), the BDI Team has defined the following key research objectives:

- **Data centralization**: To centralize and disseminate data from the EPIC study and other related research.
- **Toolbox development**: To maintain a cutting-edge suite of statistical tools designed for the analysis of contemporary epidemiological data.
- **Knowledge enhancement**: To use these tools to deepen the understanding of the interactions between socioeconomic position (SEP), lifestyle choices, and molecular factors, and their collective impact on cancer risk.

As illustrated in the chart below, the BDI Team's workplan is concentrated on three main research areas:

1. Enhancing research and methodology
2. Molecular epidemiology
3. Lifestyle and cancer



Governance

The governance of the BDI Team is organized through monthly hybrid meetings, weekly meetings with the administrative assistant and the Epidemiology and Cancer Virology Section (ECVS), and ad hoc meetings with research assistants. A dedicated Team channel has been established to facilitate communication. Team-building activities were held in 2022, 2023, and 2024, and regular lunch gatherings are organized to foster camaraderie.

Workplan progress

Projects and consortia

The BDI Team is actively involved in a variety of international projects, including:

MeDiCa; DISCERN; ColoMARK; SOMA-scan; LIBERTY; SILICA; ILIAD; LIFELONG; SISCan; ShapeCancer; ShapeSurv; AdCoSurv; ComoCanS; ABC-MeHT; OPICO-NIH

Applications and grants

Funding: The BDI Team operates with the support of 17 active grants, serving as the coordinator for 13 and as a partner for 4. These grants are sourced from organizations such as WCRF, EC, ANR, ICL, INCA, LNCC, and NIH, contributing a total budget of about €4.5 million (~€550,000 available each year).

Future grants: The BDI Team anticipates securing 9 additional grants in the near future.

Publications

See "Key publications" below.

Training

The BDI Team is involved in several training sessions, including:

- **IARC Summer School:** Coordination by NME with lectures, in collaboration with the LCB.
- **Collaborative training with GEM and LCB**:
  - Tidyverse Fundamentals with R: Modern data manipulation and visualization in R.
  - Multivariate Analysis for -Omics Data Integration: Principles and applications, organized with the Swiss Institute of Bioinformatics (SIB).
  - Introduction to Multiple Imputation for Missing Data.
  - FAIR Data Principles in Practice.
  - Data Visualization with R Shiny.
- **Machine learning course:** Offered at EM Lyon.
- **IARC Statistics working group seminars:** 21 seminars conducted since February 2021.
- **Working groups:** Coordinated by Vivian Viallon and Pietro Ferrari.

Key collaborations

Cooperation across IARC Branches

Although the BDI Team does not engage in formal collaborations with other Branches, it plays a transversal role within the NME Branch, interacting with all NME teams. The BDI Team has collaborative projects with GEM scientists, including DISCERN and OPICO, although GEM is not represented within the BDI Team. In addition, the BDI Team provides ad hoc statistical support to other branches, including ENV and CSU.

Collaboration with external partners

- EPIC: Collaborators from Imperial College London (M. Gunter, E. Riboli, D. Muller), Oxford University (T. Key, R. Travis, K. Smith-Byrne), and CESP (G. Severi, A. Thiebaut, T. Truong).
- NCI: E. Loftfield, S. Smith-Warner.
- Japan Public Health Center-Based Prospective (JPHC) Study and St Luke's International Hospital Cohort Study: N. Sawada, T. Kimura.
- Melbourne Collaborative Cohort Study (MCCS): D. English, G. Dashti, R. Milne, H. Jayasekhara.
- Physical Activity and Obesity: M. Leitzman, H. Baurecht (Regensburg), T. Duarte Salles (IDIAP JGol), B. Fervers (CLB), J. Bowden (Exeter).
- AI/ML/Statistics: M. Chadeau-Lyam (ICL), J. Chiquet (AgroParisTech), Y. de Castro (ECL), L. Serio (CERN), C. Proust-Lima (Bordeaux), Y. Chen (UPenn).
- Networks: Participation in the DISCERN and ColoMARK networks.

Main innovations

Methodological development: The BDI Team is dedicated to advancing methodological research and maintaining robust computing and statistical infrastructure to support and enhance research initiatives.

A key responsibility of the BDI Team is the **centralization of data within the EPIC study**. This includes:

- Centralizing updates on vital status and cancer end-points.
- Centralizing follow-up dietary questionnaire data.
- Centralizing molecular data to be collected in EPIC over the coming years.

In addition, the BDI Team will coordinate the **centralization of data for studies conducted in LMICs**, including the SABC, EDSMAR, and PRECAMA studies led by NME, as well as large European projects such as DISCERN and PROMINENT (led by GEM).
Data sharing solutions: An important innovative aspect of the BDI Team's work is developing solutions to share these data with external collaborators while ensuring compliance with data protection regulations and FAIR principles. This will be achieved through collaboration with the IARC Scientific IT platform.

Contributions to MTS implementation

Fundamental priorities
The work programme of the BDI Team aligns seamlessly with the priorities of the MTS:

- ➔ **Understanding the causes of cancer** (Level 3 Project Tree: 2.1; 2.2).
- ➔ **Strengthening the efficiency and effectiveness of the Agency's research and collaboration** (Level 3 Project Tree: 6.1).

Main challenges

The primary challenges facing the BDI Team include:

- Difficulty in **recruiting postdoctoral researchers** with the necessary background or skills in statistics.
- **Administrative burdens**, particularly related to project management and data sharing/access.

Next steps

The BDI Team has outlined the following next steps for its development:

- ➔ Enhance **interactions within the Team.**
- ➔ Achieve a better **balance between administrative/support tasks and research activities**.
- ➔ Concentrate on a **narrower set of topics**.
- ➔ Explore **federated analyses**.

RECOMMENDATIONS

The BDI Team has demonstrated high productivity in terms of grants, publications, and training. To further strengthen its effectiveness, the following recommendations are made:

- ✓ Incorporate GEM, CSU, and LCB as Team members to better reflect existing collaborations, or designate GEM as a co-leader to signify the level of collaboration.
- ✓ Consolidate partnerships with the IARC Scientific IT platform.

Key publications

- Viallon V, His M, … , Ferrari P. A New Pipeline for the Normalization and Pooling of Metabolomics Data. Metabolites. 2021; 11 (9).

- Loftfield E, Stepien M, Viallon V, …, Ferrari P. Novel Biomarkers of Habitual Alcohol Intake and Associations with Risk of Pancreatic and Liver Cancers and Liver Disease Mortality. J Natl Cancer Inst. 2021.
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- Ballout N, Garcia C, Viallon V. Sparse estimation for case-control studies with multiple disease subtypes. Biostatistics. 2021; 22 (4): 738-755.
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- Breeur M, Stepaniants G, Keski-Rahkonen P, Rigollet P, Viallon V. Optimal transport for automatic alignment of untargeted metabolomic data. eLife 2024.
- Jansana A, Viallon V, ….., Freisling H. Impact of pre-existing cardiometabolic diseases on metastatic cancer stage at diagnosis: a prospective multinational cohort study. Cancer Communications 2024.
- Botteri E, Peveri G, …, Ferrari P. Lifestyle changes in middle age and risk of cancer: evidence from the European Prospective Investigation into Cancer and Nutrition. Eur J Epidemiol. 2024.
- Matta K, Viallon V, …, Ferrari P. Healthy Lifestyle Change and All-Cause and Cancer Mortality in the European Prospective Investigation into Cancer and Nutrition Cohort. BMC Med. 2024.

References

- Webpage of the BDI Team

Cancer Inequalities (CIN) Team

Innovations Teams
➔ Starting date: March 2021

Members

Team leader: Dr Salvatore Vaccarella (Scientist, CSU)

Team members: The CIN Team consists of 10 members from the CSU Branch as mentioned below, as well as collaborators in others Branches: Dr Valerie McCormack (ENV), Dr Heinz Freisling (NME), Dr Pietro Ferrari (NME), Dr Komodo Matta (NME), and Mr Damien Georges (EPR).

➔ Dr Marzieh Eslahi (Postdoctoral Scientist, CSU); Dr Maxime Large (Postdoctoral Scientist, CSU); Dr Margherita Pizzato (Visiting Scientist, CSU); Dr Sébastien Lamy (Visiting Scientist, CSU; INSERM, Toulouse, France); Dr Valentina Lorenzoni (Visiting Scientist, CSU; Sant'Anna University, Pisa); Mr Mohamed Youcef Ali (Master's Student, CSU); Dr Freddie Bray (Branch Head, CSU); Dr Hadrien Charvat (Visiting Scientist, Scientific Consultant, CSU); Dr Olga Trusova (Visiting Scientist, CSU); Dr Serra Kerman (postdoctoral scientist/project manager)

Objectives

The CIN Team has four main objectives:

1. Addressing socioeconomic inequalities in health

The need to reduce socioeconomic inequalities in health and cancer is increasingly recognized as a matter of social justice and human rights. It is also acknowledged as beneficial from an economic perspective, making it a priority in public health agendas and the Sustainable Development Goals.

2. Understanding social inequalities in cancer

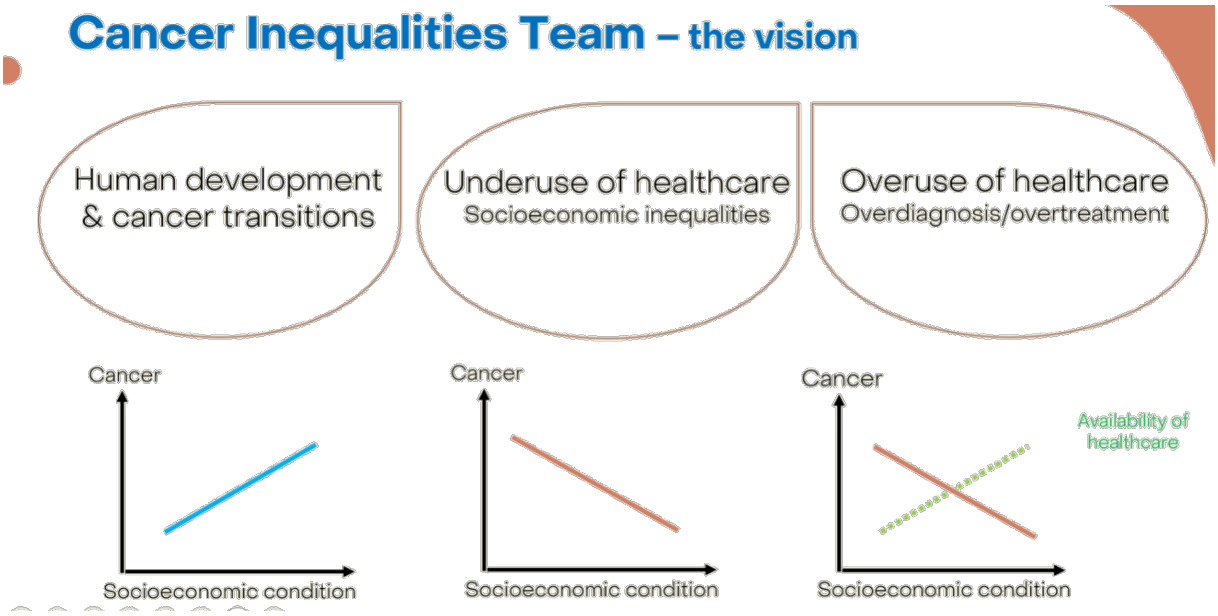
Social inequalities in cancer remain a critical public health issue, affecting all individuals but disproportionately affecting the most disadvantaged groups. These inequalities have significant financial repercussions for societies and profoundly influence health outcomes. Understanding how these inequalities evolve over time necessitates a comprehensive perspective that considers economic, social, political, legislative, and technological forces. These factors shape the distribution of risk factors within populations and influence access to health-care services, which contributes to the observed disparities in cancer outcomes. Moreover, psychosocial factors often lead individuals of lower socioeconomic status to adopt unhealthy behaviours, exposing them to a greater variety and intensity of cancer risk factors compared with their more advantaged counterparts. To monitor, investigate, and address these issues effectively, high-quality data on populations are essential, requiring multisectoral action to develop effective solutions to social inequalities in cancer. Research plays a vital role in providing the necessary data to inform evidence-based interventions aimed at reducing these inequalities (IARC Scientific Publication No. 168).

3. Measuring and monitoring inequalities in cancer

The CIN Team aims to measure and monitor social inequalities in cancer incidence, survival, and mortality, recognizing that these disparities vary across different populations. The social gradient in cancer reflects complex patterns both between and within countries, driven by a multifaceted interplay of factors. The Team's objectives include comparing these inequalities across populations within the broader context of the global epidemiological transition of cancer, while also addressing inefficiencies in healthcare provision, such as overdiagnosis.

4. Clarifying mechanisms behind inequalities

The CIN Team is committed to elucidating the mechanisms – particularly the structural determinants of health – behind social inequalities in cancer. This includes examining factors at all levels (individual and contextual, proximal and distal) and along the entire cancer continuum, from risk factors and prevention to early detection and treatment.



Workplan progress

Projects and consortia

The members of the CIN Team are actively engaged in eight scientific consortia, with IARC acting as Principal Investigator (PI) in three of them: EUCanIneq, Socineq, and Thycost. The CIN Team emphasizes its involvement in European projects, including:

- EUCanIneq (PI)
- UNCAN.eu (Task Leader)
- EUCervScreen (Work Package Leader)

Applications and grants

Since 2021, the CIN Team has successfully contributed to nine grant applications, securing a total of €1.328 million in funding for IARC. The details of the projects are as follows:

Governance

The leader of the CIN Team indicated that regular discussions take place with Team members, whether in person or via teleconference. These meetings also include visiting scientists who are based outside of IARC.

Collaboration with WHO

The CIN Research Team has collaborated with the WHO Regional Office for Europe on the publication titled **"Childhood Cancer Inequalities in the WHO European Region."** In addition, Team members have analyzed incidence rates across countries as part of the WHO Cervical Cancer Elimination Initiative.

Project	Role	Period	Grant Amount
EUCanIneq	PI	Feb 2023 to May 2025	€600,000
UNCAN.eu	Task Leader	Sept 2022 to Nov 2023	€54,000
EUCervScreen	WP Leader	Sept 2023 to Aug 2026	€21,000
Cancerfonden	PI	Until February 2024	€120,000
Socineq/INCa	PI	Until November 2027	€263,000
Meta-thyr/INCa		Until March 2027	€60,000
Silica		Ended May 2023	€42,000
SISCanS			€40,000
Thycost/INCa	PI		€128,000

Publications

Since 2020, the CIN Team has produced 44 articles (including two currently under revision), with 22 authored as first, last, or corresponding authors. Of these publications, 29 specifically address social inequalities in cancer. The Team's work has appeared in several high-impact journals (see "Key publications" below).

Key collaborations

Cooperation across IARC Branches
The CIN Team primarily relies on scientists from the CSU Branch but maintains close collaborations with other Branches, particularly with NME in Pillar 2 and EPR and ENV in Pillar 3.

Collaboration with external partners
The CIN Team has a broad network of scientific partners, which includes prominent institutions such as Erasmus MC in the Netherlands and Imperial College London and UCL in the United Kingdom, among others.

Training

Training is a crucial component of the CIN Team's activities. The Team Leader ensures that members participate in various training opportunities, including:

- External courses:
  - "Introduction to Multiple Imputation for Missing Data" (Victorian Centre for Biostatistics)
  - CLADAG School on Statistical Methods for Unsupervised and Supervised Learning (Italian Statistical Society)
  - Courses on Medical Statistics (University of Milan)
  - Systematic Reviews and Meta-Analyses (University of Milan)
  - Economic Evaluation of Public Health Interventions (EUPHA Public Health Economics Section)
- Internal courses:
  - "Statistical Practice in Epidemiology using R"
  - IARC Summer School
  - Training on Childhood Cancer Registration

Routine internal training is also conducted informally on topics relevant to descriptive cancer epidemiology, such as age-period-cohort models and survival analysis techniques.

Invited talks and events

Members of the CIN Research Team have contributed to various invited talks and events, including:

- Cancer Prevention Research Conference (June 2024, CRUK, NCI, ACS, Boston, USA) – Chairing the session on health inequities in cancer incidence and prevention
- Thyroid Cancer Conference (November 2023, Verona, Italy)
- Breast Cancer Conference (October 2023, Montpellier, France)
- Guangdong Outstanding Overseas Teacher Program (October 2023, China)
- ECO High-Level Meeting (June 2023, Brussels, Belgium)
- IPV Conference (April 2023, Washington DC, USA)
- Columbia University (April 2023, New York City, USA)
- Imperial College London (March 2023, virtual)
- World Cancer Conference (October 2022, Geneva, Switzerland)
- American Thyroid Association (October 2021, virtual)

Main innovations

The CIN Team addresses the paradox within healthcare systems, focusing on both the underutilization of healthcare services and preventive measures by individuals with low socioeconomic status and the overuse of low-value care among those with greater access to health services. This dual focus highlights the need for equitable healthcare practices. In collaboration with ENV, the CIN Team studies the consequences of maternal orphanhood due to cancer, revealing a cycle of disadvantage and poverty. The CIN Team has contributed to various policy reports on cancer, including recommendations on the overdiagnosis of thyroid cancer, which have led to significant changes in guidelines and clinical practices informed by IARC's research.

At the European level, the CIN Team has played a pivotal role in several key initiatives, such as:

- **The European Cancer Inequalities Registry**
- **The UNCAN.eu project**, particularly Work Package 6 on Inequalities in Cancer Research
- **The WHO Regional Office for Europe report on "Childhood Cancer Inequalities in the WHO European Region"**

Contributions to MTS implementation

Fundamental priorities

➔ The research on cancer inequalities is a significant topic under the first fundamental priority of IARC's MTS: "Data for Action". It aims to enhance understanding of the causal pathways linking social disadvantage to health disparities and to support countries in collecting data to better describe cancer disparities globally. The CIN Team's work contributes directly to this initiative and should foster stronger collaborations with other scientific Branches, particularly those focused on nutrition and environmental influences on cancer.

Emerging priorities

➔ Cancer inequalities are a critical component of the third emerging priority of the MTS 2021–2025, focusing on the "Economic and Societal Impacts of Cancer." The MTS states that "the cancer burden is not equally distributed across countries, within countries, and between different groups within societies." Structural determinants of health, including social and economic conditions, produce significant social gradients in cancer incidence, survival, and mortality. IARC is well-positioned to address these issues through its capability to catalyze research partnerships and analyze international studies.

Main challenges

The CIN Team aims to elevate cancer inequalities from an "emerging priority" in the MTS 2021–2025 to a fundamental priority in future iterations of the strategy. To achieve this, the Team must define strategies to enhance IARC's leadership and impact in this domain, including strengthened fundraising efforts and collaboration with key partners such as the OECD. Key points emphasized by the Team leader include:

- The CIN Team is already recognized as a leader in the fields of social inequalities in cancer and overdiagnosis, as evidenced by numerous high-impact publications and invitations to major conferences. These topics are likely to gain further importance in the global agenda and at IARC; however, sustaining or expanding this high-level focus is challenging with reliance on temporary staff funded by grants.
- Having even a part-time, fixed-term data manager/statistician could ensure continuity in the CIN Team's activities over time.
- Although the CIN Team has successfully secured project-specific funding, long-term support is necessary to maintain its position and facilitate growth.

Next steps

The CIN Team leader plans to develop scientific projects focused on:

➔ The field of cancer inequalities.
➔ The issue of overdiagnosis in cancer.

RECOMMENDATIONS

✓ The CIN Team should strengthen cross-cutting collaborations within IARC and integrate members from outside the CSU Branch.
✓ The Team leader should consider establishing a co-leadership structure with scientists specializing in implementation research from the EPR Branch to enhance the effectiveness of the Team's efforts.

Key publications

- Malagón T, Franco EL, Tejada R, Vaccarella S. Epidemiology of HPV-associated cancers past, present and future: towards prevention and elimination. Nat Rev Clin Oncol. 2024 Jul;21(7):522-538. Epub 2024 May 17. PMID: 38760499 Review.
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References

- Webpage of the CIN Team
- IARC Scientific Publication No. 168: Reducing Social Inequalities in Cancer: Evidence and Priorities for Research
- World Cancer Report Webinar Series, Social inequalities and cancer

Rare Cancer Genomics (RCG) Team

Innovations Teams
➔ Starting date: July 2021

Members

Team leaders: Dr Lynnette Fernandez-Cuesta and Dr Matthieu Foll, Genomic Epidemiology Branch (GEM)

Team members: The CCG Team comprises 8 members within the GEM Branch: 3 scientists; 1 research assistant; 2 postdoctoral scientists, and 2 PhD students. It relies on multidisciplinary expertise, combining biology/biochemistry, computational biology, statistics, bioinformatics, and machine learning/AI.

- ➔ Dr N Alcala (Scientist, GEM); Dr A Sexton-Oates (Scientist, GEM); Dr L Mangiante (Scientist, GEM); Dr C Voegele (Research Assistant, GEM); Dr E Mathian (Postdoctoral Scientist, GEM); Dr L Bonheme (Postdoctoral Scientist, GEM); Ms G Drevet (PhD Student, GEM); Ms L Mange (PhD Student, GEM).
- ➔ The Team includes visitors hosted by IARC in 2024: E Lauricella, Policlinico di Bari, Italy (18 months); L Kalson, Medical University Graz, Austria (4 months); I Urbarova, The Arctic University, Norway (2 weeks).

Objectives

The primary goal of the RCG Team is to elucidate the molecular characteristics of rare cancers in order to better understand their etiology and carcinogenesis processes. Ultimately, the team aims to enhance clinical management and improve the prognosis for patients. The Team primarily concentrates on three types of rare cancers: mesotheliomas, lung neuroendocrine neoplasms, and sarcomas.

To support this objective, the RCG Team focuses on intercepting rare cancers—catching cancer cells at their nascent stage, when they are developing into pre-cancers or very early cancers, in order to halt or reverse their progression. The Team uses several approaches to achieve these goals:

- ➔ **Integrative multi-Omics analyses**: Conducting comprehensive molecular analyses of large biorepositories that contain high-quality samples with detailed pathological, clinical, and epidemiological annotations.
- ➔ **Big data integration**: Merging data generated from various large-scale genomics initiatives to facilitate the translation of research findings into tumour classification.
- ➔ **Morphological characterization**: Using image-based deep learning to identify new morphological characteristics and integrating these findings with molecular data.
- ➔ **In vitro organoid models**: Using advanced in vitro organoid models to investigate cancer initiation and progression, in collaboration with external partners.

Workplan progress

Projects and consortia

The RCG Team is involved in several key networks, including:

- **European Neuroendocrine Tumour Society (ENETS)**
- **European Reference Network on Rare Adult Solid Cancers (EURACAN)**
- **European Prospective Investigation into Cancer and Nutrition (EPIC)**
- **French MESOBANK**
- **Réseau National Expert pour le Mesothéliome Pleural Malin (NET MESO)**
- **Lung NEN Network**

Applications and grants

- **MESOMICS:** The RCG Team currently holds 7 active grants for the MESOMICS project, totaling €1,277,500. The primary funders include: Institut national du Cancer in France (INCa); Worldwide Cancer Research; Agence Nationale de Recherche (ANR); Ligue contre le Cancer. Pending outcomes from ANR Chairs of Excellence and NIH R01.

- **LungNENomics:** The RCG Team has 9 active grants for the LungNENomics project, amounting to €1,701,000.
- The main funders are NIH; Dutch Cancer Society; Worldwide Cancer Research; Institut national du Cancer in France (INCa); Ligue contre le Cancer; Neuroendocrine Tumour Research Foundation. Pending outcomes from NETRF; Mark Foundation; INCa LABREX; To be submitted to ERC CoG.
- **SARCOMICS:** This project received an A score in the ERC CoG application but remains unfunded.
  It has partial funding from ANR T-ERC and LYriCAN+. Pending outcomes from WCR and NIH R0. Total Funds Raised: more than €3,300,000 since 2021.

Key Publications

The following is a summary of the top publications by the RCG Team for each project (see "Key publications" below for detailed list):

MESOMICS: 5 publications since 2021

- ➔ 2 leading original papers, including 1 with an Impact Factor (IF) > 10
- ➔ 2 leading review papers, including 1 invited review with an IF > 30
- ➔ 1 paper submitted to *Science*

Invited Speakers/Oral Presentations:

- 2024 BioSyl Computational Biology of Cancer
- 2023 EMBL Cancer Genomics Conference
- 2023 VarICOSI ISMB/ECCB
- 2023 16th International Conference of the International Mesothelioma Interest Group (iMig)
- 2022 IASLC World Conference on Lung Cancer
- 2021 Virtual 15th International Conference of the International Mesothelioma Interest Group (iMig)
- 2021 Virtual IASLC 2020 IASLC World Conference on Lung Cancer

LungNENomics: 14 publications since 2021

- ➔ 5 leading original papers, including 1 with an IF > 50
- ➔ 3 leading review papers, all invited, including 1 with an IF > 10
- ➔ 4 co-author papers, including 1 with an IF > 10
- ➔ 2 publications as experts in collaboration with the WHO Classification of Tumours programme

Dr Fernandez-Cuesta contributed as expert co-author to the Neuroendocrine Tumours chapter of the WHO Classification of Thoracic Tumours, 5th edition, 2021 (collaboration with IARC-WCT).

Invited Speakers/Oral Presentations:

- 2023 EMBL Cancer Genomics Conference
- 2023 NETRF Research Symposium
- 2023 IASLC World Conference on Lung Cancer
- 2023 ASCO Annual Meeting
- 2023 European Congress of Endocrinology

Governance

Internal meetings: Weekly Team meetings to discuss project updates, manuscript progress, troubleshooting, authorship, and emerging opportunities.
External meetings: Monthly project-specific meetings with Team members and external collaborators to review progress on outsourced tasks. Annual Computational Genomics Workshop to enhance collaboration and knowledge sharing.

Dr Fernandez-Cuesta oversees administrative tasks, including CRAs, APWs, MTAs, DTAs, meeting planning, agendas, minutes, internal communications, grant management, scientific and financial reporting, and team budgeting. Dr Foll manages IT responsibilities, encompassing EGA DTAs, Twitter engagement, data management, bioinformatics, and project management tools.

Links with WHO
The RCG Research Team has synergies with the WHO Classification of Tumours programme; however, no specific collaborations with WHO headquarters or regional offices have been noted.

- 2023 20th Annual ENETS Conference
- 12th European Meeting on Molecular Diagnostics
- 2022 IASLC World Conference on Lung Cancer
- 1st World NET Forum 2022 – Annual ENETS Conference
- 2021 18th Annual ENETS Conference

Training

The leaders of the RCG Research Team have contributed to various training and teaching activities:

- **Cancer genomics courses:** Conducted at INSA and the Master in Cancer Genomics, University of Pavia, Italy.
- **Computational biology courses:** Various sessions offered.
- Plans to establish a **Cancer Genomics Summer School**.
- **Short internships:** Six ECVS members joined the team for short internships (2-6 months), funded by their institutions. Most produced manuscripts with RCG Team members as co-authors.
- **Mentorship programme:** Ongoing support for team members.
- **Computational cancer genomics annual workshop:** Scheduled for November 2024.
- **Alumni:** 11 Master's students, 5 PhD students, and 4 post-doctoral have participated in programmes.

In 2022, Dr Fernandez-Cuesta and Dr Foll became chairs of the EPIC Rare Cancers Working Group. They developed a centralized database that summarizes all rare cancer cases in EPIC, providing user-friendly access to epidemiological and clinical data, as well as biological specimens available.

Key collaborations

Cooperation across IARC Branches
The RCG Research Team primarily collaborates with personnel from the GEM Branch while maintaining close interactions with other scientific Branches, particularly:

- **Pillar 2:** NME
- **Pillar 3:** EGM
- **Pillar 4:** WHO Classification of Tumours programme (ESC Branch) and LCB.

These collaborations are not currently reflected in the composition of the Team. Ongoing discussions aim to strengthen cooperation with the IARC Team focused on childhood cancer.

Collaboration with external partners
The RCG Research Team actively engages in scientific collaborations within large cohort consortia, partnering with organizations such as:

- European Neuroendocrine Tumour Society (ENETS)
- European Reference Network on Rare Adult Solid Cancers (EURACAN)
- European Prospective Investigation into Cancer and Nutrition (EPIC)
- French MESOBANK
- Réseau National Expert pour le Mesothéliome Pleural Malin (NET MESO)
- Lung NEN Network
- Centre Léon Bérard/CRLC
- HCL
- CHU in France
- Various international universities

In addition, the RCG Research Team contributes significantly to the local SIRIC LYriCAN+ programme, supported by INCa, in collaboration with CRCL, CLB, and HCL.

Main innovations

- **Innovative multimodal computational research approaches**: The RCG Team uses advanced methodologies to enhance research efficacy.
- **Deep learning and AI applications**: Since 2021, the Team has used deep learning and artificial intelligence to address unresolved questions, including a collaboration with Owkin.
- **International multidisciplinary open-science efforts**: The team is committed to open science principles, which include:
  - Open research data
  - Open-source software and source code
  - Open access to publications
  - Open education
  - Training and professional development for personnel

Contributions to MTS implementation

Fundamental priorities
The RCG Research Team significantly contributes to the following fundamental priorities of the MTS 2021-2025:

- ➔ **Objective 2.2**: Enhance understanding of and elucidate the biological mechanisms of carcinogenesis relevant to environmental and lifestyle factors, particularly those accompanying key cancer transitions and addressing cancer disparities through laboratory studies.
- ➔ **Objective 4.2**: Strengthen the understanding and application of tumour classification to support cancer diagnosis, management, and research.

Main challenges

The RCG Team faces several challenges, including:

- **Funding and publication difficulties**: Challenges associated with securing funding and publishing research on rare cancers.
- **Perception issues**: The pioneering and disruptive nature of the RCG Team's research is sometimes met with resistance.
- **Alignment with IARC priorities**: The RCG's Team research may be perceived as not aligning with IARC's overall priorities.
- **Recognition and career opportunities**: A lack of recognition can limit career advancement for team members.

Next steps

The leaders of the RCG Team have outlined the following next steps for the research team:

- ➔ **Development of additional epidemiological studies**: Focused on investigating the etiology of rare cancers within the EPIC cohort.
- ➔ **Expansion of the Shiny app**: Extend its functionality to encompass all cancers in the EPIC study.
- ➔ **Establishment of a Junior Team**: Focused on artificial intelligence and cancer research.
- ➔ **Creation of a cancer registry for mesothelioma**: To be implemented in LMICs in collaboration with CSU.
- ➔ **Broaden research focus**: Expand from rare cancers to include studies on cancer evolution, ecology, and deep learning.
- ➔ The RCG Team is currently being renamed to the **Computational Genomics Team (CCT)** to better reflect its evolving focus.

RECOMMENDATIONS

The RCG Team is dynamic and productive, demonstrating strong organizational skills in governance and training. Its innovative approaches, including deep learning and AI, have the potential to enhance research activities in other branches, such as NME and EPR.

- ✓ The RCG Team is currently situated within the GEM Branch; however, its composition does not adequately reflect the synergies with other Branches, including NME, EGM, and the WHO Classification of Tumours Programme (ESC).
- ✓ The Team's commitment to Open Science, championed by Dr Foll, aligns with one of the Agency's key focuses.
- ✓ Given the Team's primary focus on the molecular characterization of super-rare cancers to inform classification and tertiary prevention, the Team leaders should engage in discussions with the Branch Head and DIR to ensure that this research aligns with GEM's priorities and the new scientific strategy for 2026-2030.

Key publications

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- Moonen L, Mangiante L (co-first), Leunissen DJG, Lap LMV, Gabriel A, Hillen LM, Roemen GM, Koch A, van Engeland M, Dingemans AC, Foll M, Alcala N, Fernandez-Cuesta L (co-last), Derks JL, Speel EM. Differential Orthopedia Homeobox expression in pulmonary carcinoids is associated with changes in DNA methylation. Int J Cancer. 2022
- Mc Leer A et al. Detection of acquired TERT amplification in addition to predisposing p53 and Rb pathways alterations in EGFR-mutant lung adenocarcinomas transformed into small-cell lung cancers. Lung Cancer. 2022
- Gabriel AAG, Mathian E, Mangiante L, Voegele C, (…), Alcala N, Fernandez-Cuesta L, Foll M. A molecular map of lung neuroendocrine neoplasms. Gigascience. 2020
- Reviews
- Fernandez-Cuesta L, Alcala N, Dayton T, Malanchi I, Perren A, Walter T, Foll M. Invited review on NENs due in July 2024 JCI. IF 15.9
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References

- Webpage of the RCG Team
- Individual webpage of the RCG Team

Hormones and Metabolism (HorM) Team

Innovations Teams
➔ Starting date: January 2021

Members

Team leaders: Dr Sabina Rinaldi (Scientist, Deputy Branch Head) and Dr Laure Dossus (Scientist), Nutrition and Metabolism Branch (NME)

Team members: In addition to the 2 leaders, the HorM Team comprises 15 members within the NME Branch: 6 post-doctoral scientists, 2 PhD students, 1 statistical assistant, 2 laboratory assistants, 1 secretary, and 1 visiting scientist. The HorM Team relies on multi-disciplinary expertise, combining biochemistry, cancer epidemiology, nutrition, and statistics.

➔ Postdoctoral scientists: Dr Esther Gonzalez Gil (NME); Dr Sabrina Wang (NME); Dr Yahya Mahamet-Saleh (NME); Dr Rola Jaafar (IARC Postdoctoral Fellow, NME); Dr Azam Majidi (NME); Dr Sanam Shah (IARC Postdoctoral Fellow, NME); PhD students: Ms Fanélie Vasson (NME); Ms Yadi Zheng (NME); Statistical assistant: Ms Carine Biessy (NME); Laboratory assistants: Ms Anne-Sophie Navionis (NME); Ms Béatrice Vozar (NME); Secretarial support: Ms Karine Racinoux (NME); Visiting Scientist: Dr Agnès Fournier (NME).

Objectives

The HorM Team is dedicated to advancing research on the role of hormones and metabolism in cancer etiology, building upon established molecular epidemiology research focused on hormone-dependent cancers. The team uses cutting-edge laboratory technologies in conjunction with epidemiological studies in high-income settings and countries undergoing epidemiological transitions.

The HorM Team's ongoing and future activities include:
- **Laboratory methodology**: Supporting the NME Branch and IARC research by developing advanced laboratory methodologies.
- **Identification of modifiable risk factors**: Investigating factors that influence cancer development and survival in understudied populations.
- **Discovery of novel risk factors**: Exploring new risk factors associated with hormone-related cancers.
- **Obesity and metabolic health**: Using molecular tools to understand causal pathways between obesity, metabolic health, and cancer.
- **Evaluation of biological mechanisms**: Assessing the biological mechanisms that link diet, lifestyle, and cancer as part of the Global Cancer Update Programme.

Research focus

- **In high-income settings**: Development of studies through collaborations with existing cohorts to leverage available data and resources.
- **In countries undergoing epidemiological transition**: Implementation of targeted population-based case-control or cross-sectional studies to better understand population-specific risk factors.

The specific activities of the HorM Team encompass:

- **Laboratory methodologies**: Research involving sex steroids, hormones, fatty acids, polyphenols, targeted metabolomics using the Biocrates AbsoluteIDQ® p180 kit, and immunoassay-based proteomics.
- **Identification of risk factors**: Focused research on modifiable risk factors affecting cancer development and survival in populations that are often understudied.
- **Discovery of novel risk factors**: Ongoing investigations to identify new risk factors for hormone-related cancers.
- **Analysis of molecular pathway**: Using molecular tools to investigate the causal pathways linking obesity, metabolic health, and cancer.
- **Evaluation of diet and lifestyle factors**: Conducting research to understand how diet and lifestyle factors influence cancer risk within the framework of the Global Cancer Update Programme.

Workplan progress

Projects and consortia

The HorM Team collaborates within several key networks, including:

- **EPIC**
- **SABC**
- **PRECAMA**
- **EDSMAR**
- **KOR**
- **E3N**
- **WCRF**, CUP Global experts, and various collaborators

Applications and grants (since 2021)

The HorM Team has submitted a total of 51 applications:

- 31 rejections
- 14 grants gunded:
  - 4 as Principal Investigator (PI)
  - 10 as partners
  - Funding sources include INCa, WCRF, CRUK, and ZA-NSF.
  - Success rate: about 30%
- 6 Pending applications (currently in the full application stage): WCRF, INCa, NCI

In addition, 9 applications were submitted by HorM Team ECVSs:

- 2 rejections
- 2 mobility grants funded: CLARA, Es-MoScience (Spain)
- 1 postdoctoral fellowship funded: Fondation ARC
- 1 PhD fellowship funded: LNCC
- 1 award: Fondation l'Oréal
- 2 pending applications (currently in the full application stage): WCRF INSPIRE

The team successfully secured 2 IARC Postdoctoral Fellowship applications and 4 Direct Funding opportunities.

Governance

The governance of the HorM Team includes a variety of structured meetings and activities to facilitate communication and collaboration:

Monthly Team meetings:

- Administrative updates
- Scientific news
- News from the labs
- Updates from ECSA
- Current activities in HorM (round table discussion)
- Any other business (AOB)
- Scientific presentations followed by QandA sessions

Social activities:

- Monthly after-work gatherings and social events
- One dedicated team-building day

Scientific engagement:

- Weekly scientific presentations to promote knowledge sharing
- Bi-weekly meetings among team leaders
- Regular bilateral meetings with all personnel
- Monthly meetings with HorM-OMB lab personnel
- Project-specific meetings as required

Summary of Grants (2021-2024):

- Grants as PI: €1,555,310
- Grants as partner: €1,925,200
- Fellowships/mobility grants: €224,000
- Direct funding: €593,877
- ➔ Total funding: €4,298,387

Publications (see "Key publications" below for details):

Since 2021, the HorM Team has achieved notable success with:

- **89 Peer-reviewed publications**:
  - 17 authored by team leaders as first or last authors.
  - 5 authored as second authors.
- **H-index**:
  - Dr Sabina Rinaldi: 103
  - Dr Laure Dossus: 58

- **Impact factor statistics**:
  - 56 publications with an Impact Factor (IF) > 5.
  - 14 publications with an IF > 10.
  - 2 publications with an IF > 40.

Key collaborations

Cooperation across IARC Branches
The HorM Team primarily collaborates with personnel from the NME Branch, while also reporting strong interactions with the following Teams:

- **Onco-Metabolomics (OMB) Team**
- **Biostatistics and Data Integration (BDI) Team**
- **Lifestyle Exposure and Interventions (LEI) Team**

In addition, the HorM Team engages in synergies with other IARC Branches, including:

- **GEM:** Collaborations on BRIDGE
- **EPR**: Focused on biomarkers for early detection of breast cancer
- **ENV** Involvement in the ABC-DO initiative
- **IARC Handbooks programme**: Contributions to developing guidelines

The HorM Team also interacts with the IARC breast cancer working group and the Biobank and Laboratory Steering Committee.

Collaboration with external partners
The HorM Team engages in significant scientific collaborations primarily through large cohort consortia and population-based case-control studies. Notable international partnerships include:

- **EPIC**: Prospective cohort study in Europe
- **SABC**: Case-control study in South Africa
- **PRECAMA**: Multicentre case-control study in Latin America
- **EDSMAR**: Case-control study in Morocco
- **Kandahar Obesity Research (KOR)**: Cross-sectional study in Afghanistan

Collaborations with:

- **ICL**: M. Gunter, M. Kyrgiou
- **Bristol University**: N. Timpson, V. Tan
- **Manchester University**: E. Crosbie
- **St Luke's Tokyo**
- **WCRF**: CUP Global experts and collaborators
- **Harvard TH Chan**
- **NHI**
- **Cancer Council, Victoria**

Local and national collaborations: The team also collaborates with various local and national partners, including:

- **Centre Léon Bérard**
- **Bioaster**
- **IBCP**
- **SFR Santé Lyon Est**
- **CIRI**
- **French EPIC Cohort (E3N)**
- **EREN**
- **INSERM**
- **Network NACRe**
- **Institut Gustave Roussy**
- **Université de Rennes**
- **LABERCA**
- **Institut Paoli Calmettes, UNICANCER Marseille**

Training

The leaders of the HorM Team have contributed to various training and teaching activities, including:

- **In-house training**: Training for ECVS members, including master's students, visiting PhD students, postdoctoral scientists, and fellows.
- **Capacity-building in LMICs.**

- Dr Sabina Rinaldi:

- **2021 (online) and 2023 (on-site)**: IARC Summer School on "Molecular Epidemiology."
- **2021 (online)**: Course at the University of Antioquia, Colombia, covering topics such as:
  - "Desarrollo y utilidad de los modelos de riesgo para la prevención del cáncer de mama."
  - "Reproductive and lifestyle factors and breast cancer risk."
  - "Obesity, inflammation, and breast cancer risk."
- **2021**: Guest lecturer at Master biobanque ESTBB, Lyon, France:
  - "Introduction aux biomarqueurs."
  - "Dosage de biomarqueurs."
- **Public events:** Dr Rinaldi is responsible for organizing "grand public events" focused on cancer prevention in collaboration with CLB.

- Dr Laure Dossus:

- **2021 (online) and 2023 (on-site)**: IARC Summer School, "Introduction to Cancer Epidemiology" module.
- Course supervision (with Dr Pietro Ferrari) and coordination of group work.

- Dr Fanélie Vasson:

- **2024**: Teaching Associate for the Cancer Module in the University of Lyon's Master in Global Health.

- Dr Esther Gonzalez Gil, Dr Sabrina Wang, Dr Yahya Mahamat-Saleh:

- **2023 (on-site)**: Teaching Associates at the IARC Summer School.

Main innovations

- **Population-based research resources**: Availability of breast cancer research resources in South
- **Targeted approaches**: The HorM Team uses targeted strategies for cancer research in LMICs while emphasizing local capacity-building.
- **Integration of omics and epidemiology**: There is a strong interaction between traditional epidemiology and omics approaches to enhance research outcomes.
- **Complementarity of expertise**: The Team leverages diverse expertise to strengthen its research initiatives.
- **Coordination of case-control studies**: The team coordinates case-control studies on breast cancer in LMICs, including in Morocco, Latin America, and South Africa.
- **Public communication**: Effective communication with the lay public is a priority for the team.

Contributions to MTS implementation

Fundamental priorities

The HorM Team is an integral part of Research Pillar 2: "Understanding the Causes of Cancer," contributing to various aspects of the IARC MTS 2021-2025, specifically:

- ➔ **Objective 2.2**: Enhance understanding of biological mechanisms of carcinogenesis related to environmental and lifestyle factors, including those associated with cancer transitions and disparities through laboratory studies.

- **Objective 2.4**: Improve understanding of potential risk factors, particularly in under-researched populations and LMICs, and their relationship with observed cancer patterns.

Major contributions of the HorM Team to the expected outcomes outlined in the MTS 2021-2025 include:

- **Population-based research resources**: Availability of breast cancer research resources in South Africa (SABC), Morocco (EDSMAR), and Latin America (PRECAMA) through targeted studies on nutrition and metabolism.
- **Molecular studies**: Investigation of breast tumour subtypes and novel insights into the role of obesity and metabolic health in cancer development, specifically through genetic studies of adiposity subtypes and metabolites.
- **Circulating biomarkers**: Identification of circulating biomarkers (metabolites and proteins) linked to adipose tissue distribution and their application in cancer studies.
- **Causal pathway investigation**: Exploration of mediating pathways connecting obesity and metabolic health with cancer using advanced causal inference methods.

Main challenges

- **Transition to the Nouveau Centre**: Addressing the challenges associated with moving to the new IARC building.
- **Funding decline**: Navigating a decline in available funding.
- **Staff retention**: Maintaining essential skills amidst staff turnover.
- **Reliance on external funding**: The team is heavily reliant on grant funding, with 10 out of 15 Team members supported by external budgets.
- **High costs of laboratory maintenance**: Managing the financial burden of maintaining cutting-edge laboratories.
- **Funding challenges in LMICs research**: Securing funding for studies in LMICs is particularly difficult.
- **Methodology funding**: Funding for methodological research remains limited.
- **Increased administrative load**: Facing a rise in administrative responsibilities.
- **Compliance challenges**: Ensuring compliance with policies for material and data sharing, including GDPR regulations.

Next steps

The GCP Team has identified the following next steps for further research development:

- Enhance **laboratory methodologies** to support NME and IARC research.
- Develop **novel methodologies** for better characterization of hormone profiles, including sex hormone profiling and cholesterol metabolites, using low sample volumes.
- Broaden **applications of targeted metabolomics**, including microbiome studies.
- Incorporate **advanced proteomics** approaches.
- Apply methodologies to **new sample matrices**, such as FIT, DBS, and tissues.
- Focus on identifying **modifiable risk factors for cancer development and survival in understudied populations**.
- Use **molecular approaches** to pinpoint specific risk factors.
- Establish collaborations within a **PAN-African consortium**.
- Identify **new risk factors for hormone-related cancers** and explore novel factors and pathways associated with understudied subtypes, such as triple-negative breast cancers.
- Validate **novel biomarkers related to breast cancer etiology** and identify modifiable risk factors in BRCA1/2 mutation carriers.
- Investigate the **relationships** between thyroid disease, thyroid hormones, and ovarian cancer risk, as well as the connection between diabetes, metabolic imbalance, and differentiated thyroid cancer risk.
- Continue research on the **role of obesity and metabolic health** in cancer development.

- ➔ Use **advanced molecular profiling techniques**, including proteomics, metabolomics, and hormonomics, to gather insights.
- ➔ Explore **comprehensive metrics** beyond body mass index (BMI), focusing on body composition and metabolic health.
- ➔ Apply **triangulation of evidence** through methods such as Mendelian randomization and studies involving patients who underwent bariatric surgery and multiomics (e.g., PROMINENT).
- ➔ Investigate **the role of nutrition and other modifiable factors in cancer development**, as part of the WCRF CUP project.
- ➔ **Strengthen ties with LEI** for alignment of research on nutritional risk factors with the high-priority recommendations list for 2025-2029.

RECOMMENDATIONS

The HorM Team is highly dynamic and productive in terms of grants and publications, demonstrating strong organization and structure in governance and training. Despite being confined to the NME Branch, the Team's composition does not fully reflect potential synergies with other Branches, particularly GEM (focused on BRIDGE, mutational signatures, and proteomics), ENV (identifying risk factors in understudied populations and ABC-DO), and EPR (biomarkers for early detection of breast cancer).

- ✓ The Team should consider integrating with the IARC initiative related to the WHO Global Breast Cancer Initiative and strengthening ties with the IARC Working Group on Breast Cancer. Combining these structures may optimize resources and knowledge sharing while enhancing communication with WHO.
- ✓ Strengthening interactions with the *IARC Monographs* programme will help align research on nutritional risk factors with the high-priority recommendations list for 2025-2029 in collaboration with LEI.

Key publications

- Sanikini H, Biessy C, Rinaldi S, Navionis AS, Gicquiau A, Keski-Rahkonen P, et al. (2023). Circulating hormones and risk of gastric cancer by subsite in three cohort studies. Gastric Cancer. 26(6):969–87. PMID:37455285
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- Dossus L, Kouloura E, Biessy C, Viallon V, Siskos AP, Dimou N, et al. (2021). Prospective analysis of circulating metabolites and endometrial cancer risk. Gynecol Oncol. 162(2):475–81. PMID:34099314

References

- Webpage of the HorM Team

Lifestyle Exposure and Interventions (LEI) Team

Innovations Teams
➔ Starting date: January 2021

Members

Team leaders: Dr Inge Huybrechts (Scientist, NME)

Team members: The LEI Team comprises 14 team members (3 postdoctoral scientists, 3 doctoral students, 4 Visiting Scientists, 1 secretary, 1 project assistant, 1 research assistant) from the NME Branch in Pillar 2. Team members are from different continents and countries, namely Belgium, Brazil, France, UK, Guatemala, India, Lebanon, Malawi, Morocco, Norway, South Africa, and Türkiye.

- ➔ Postdoctoral scientists (NME): Dr J. Blanco Lopez; Dr I. Jacobs; Dr S. M. Lizia; PhD students (NME): Ms A. Al Nahas; Mr J. Berden; Ms B. Chimera; Visiting Scientists (NME): Dr E. Faure; Dr A. Fournier; Dr M. Khalis; Dr G. Skeie; Secretary (NME): Ms K. Racinoux; Project Assistant (NME): Ms T. Wootton; Senior Research Assistant (NME): Ms G. Nicolas
- ➔ External members: PhD students : Ms Eine Koc Cakmak, Ms C. Elattabi, Ms N. Lamchabbek; Postdoctoral scientists: : Dr S. Yammine, Dr N. Kliemann.

Objectives

Context

Accumulated evidence from observational studies strongly suggests that adherence to a healthy dietary pattern, regular physical activity, reduced alcohol intake, and smoking cessation could prevent up to 40% of all cancer cases worldwide. Therefore, it is crucial for governments to prioritize cancer prevention through evidence-based strategies and interventions. However, there is an urgent need for cutting-edge research to define what constitutes a healthy diet and lifestyle for cancer prevention, because current evidence on concepts such as food processing and food biodiversity remains limited. In addition, convincing evidence regarding the feasibility, effectiveness, and sustainability of lifestyle interventions for cancer prevention is still lacking.

The LEI Team was established in 2021 with the primary objective of addressing the following two questions:

- ➔ **How feasible, effective, and sustainable are lifestyle interventions for cancer prevention?**
- ➔ **How can human and planetary health be optimized through healthy lifestyle choices?**

The overarching goal of the LEI Team is to support cohorts in developing tailored lifestyle exposure methods and indicators that investigate the co-benefits for human and planetary health, following a One Health approach. In addition, the team evaluates the feasibility and potential of sustainable evidence-based lifestyle interventions to enhance cancer research and support cancer prevention strategies. The LEI Team will particularly focus on novel lifestyle factors, including food processing, biodiversity, and circadian rhythm-related behaviours such as meal timing, sleep patterns, and overnight fasting.

The LEI Team has defined three specific objectives:

1. **Objective 1**: Study Novel Lifestyle Indicators in Ongoing Epidemiological Studies
   - Related Projects: Genomyc, POPs, ADDITIVES, EpiPhare/DiTiMed, UltraCan and UltraCam, BioHealth, Zero Hidden Hunger
2. **Objective 2**: Lead and Support the Establishment of New Observational Lifestyle-Cancer Studies
   - Related Projects: IIPAN-IARC Biobank, Bone Sarcoma - Metabol-Sarc, TOUBKAL
3. **Objective 3**: Develop and Evaluate Lifestyle Interventions
   - Related Project: LIFE-SCREEN

Workplan progress

Projects and consortia

The LEI Team coordinates or directly contributes to a variety of international projects currently ongoing, including:

- **EPIC**: European Prospective Investigation into Cancer and Nutrition.
- **IIPAN**: International Lifestyle Behaviour and Biobanking Program in Paediatric Oncology.
- **NICHE**: International Childhood Leukemia Microbiome/Metabolome Cohort, with participation in South America, Africa, and India.
- **EPICKids**: Southern European Prospective Investigation into Childhood Cancer and Nutrition, covering Spain and Italy.
- **Life-Screen**: Intervention project based in France.

Applications and grants

Since the inception of the LEI Team in 2021, its activities have been supported by grants from various organizations, including:

- Fondation de France
- World Cancer Research Fund (WCRF)
- French National Research Agency (ANR)
- French Agency for Food, Environmental and Occupational Health and Safety (ANSES)
- Institut National du Cancer (INCa)
- Cancer Research UK
- Marie Curie

➔ **Total funding since 2021**: about €2 million.
➔ **Grants as principal investigator**: 4 grants totalling €0.5 million.
➔ **Grants as co-applicant**: 6 grants totalling €1.2 million.
➔ **Postdoctoral funding**: 2 grants totalling €0.3 million.
➔ In 2023, the LEI Team submitted 13 grant applications, with 9 submitted by the team members as Principal Investigators (PIs) or co-PIs. Three applications were awarded, with 2 of those as PI or co-PI.

Governance

The governance of the LEI Team is structured as follows:

- **Monthly LEI Team meetings**: Administrative updates; presentations by team members
- **Weekly meetings**: Meetings with PhD students and first-year postdoctoral scientists
- **Biweekly meetings**: Meetings with postdoctoral scientists
- **Project meetings**: Internal meetings and meetings with consortia
- **Working groups**: Chairing and participating in various working groups and networks
- **Team-building activities**: Organized activities to strengthen team cohesion

Links with WHO

Dr Huybrechts is a member of the IARC Team focused on childhood cancer, which is related to the WHO Global Initiative. She collaborates with the Food and Agriculture Organization (FAO).

Dr Huybrechts will present alongside Dr Zisis Kozlakidis (Head of the LSB) at a side event organized by WHO (Global Initiative for Childhood Cancer) during the World Health Assembly in May 2024. IARC, WHO, and Columbia University are partners in the NICHE and EPICKids projects currently ongoing at the Agency and will play key roles in this event.

Publications

See “Key publications” below for details.

Training

Contributions to training by the LEI Team include:

- Supervision of master’s students, PhD students, and postdoctoral scientists.
- Participation in the IARC Summer School.
- Contributions to academic programmes at institutions such as Wageningen University and The London School of Hygiene and Tropical Medicine.
- Encouragement for LEI Team members to use resources provided by IARC/WHO (e.g., iLearn) for continuous learning and professional development.

Key collaborations

Cooperation across IARC Branches
The LEI Team comprises staff from the NME Branch under Pillar 2. Although the team's organizational chart does not reflect collaboration with other branches, the LEI Team actively participates in projects involving other Branches, such as:

- **CSU:** Related to childhood cancer projects.
- **Nutrition, Cancer and Multimorbidity (NCM) Team:** Led by Dr Heinz Freisling within the NME Branch.
- **EPR:** Focused on interventions and implementation research.

Collaboration with external partners
The LEI Team collaborates with various local and international stakeholders, including:

- EPIC Consortium
- BioHealth Consortium
- UPF Team and Consortium
- GenoMyc Consortium and MYCA Consortium
- HELENA and Idefics Consortia
- EXPANSE Consortium
- Zero Hidden Hunger Consortium
- European Food Safety Authority (EFSA) Collaborators

Main innovations

- **One Health approach:** The LEI Team emphasizes a One Health approach, integrating human, animal, and environmental health considerations in cancer research.
- **Climate change and cancer:** Investigating the effects of climate change, particularly the impact of ultra-processed foods on greenhouse gas emissions and cancer risk.

Contributions to MTS implementation

Fundamental priorities

The activities are also in accordance with the MTS for 2021-2025, which includes:

- **Objective 2**: Understand the causes of cancer.
- **Objective 3**: Evaluate and implement cancer prevention and control strategies.
- **Objective 4**: Increase the capacity for cancer research.

More specifically, the LEI Team's activities contribute to the following IARC MTS specific objectives:

- **Sub-objective 2.1.3**: Advancing understanding of the causes of cancer by considering dietary, metabolic, and lifestyle factors. This includes research on the potential roles of mycotoxins, food processing, and food biodiversity in relation to cancer risk, alongside exploring the mechanisms involved through the identification of metabolites and metabolic signatures associated with these dietary exposures.
- **Sub-objective 3.1.1**: The LIFE-SCREEN intervention study, integrated into the colorectal cancer screening programme in France, contributes to analyzing the effectiveness of primary cancer prevention strategies.
- **Sub-objective 3.2.1**: Identifying factors influencing the effective implementation of primary and secondary prevention programmes.
- **Sub-objective 3.1.3**: The "International Lifestyle Behaviour and Biobanking Program in Paediatric Oncology" (IARC-IIPAN) aims to establish a cohort of patients with childhood cancer across high-, middle-, and low-income settings, considering emerging lifestyle

transitions. This initiative enhances understanding of factors affecting cancer prognosis and supports the development and maintenance of research platforms (Sub-objective 4.3.1) by creating tools and protocols for large-scale international epidemiological studies, made available through an online toolbox. It also responds to emerging research opportunities (Sub-objective 4.3.3) through its collaboration with the International Initiative for Paediatrics and Nutrition (IIPAN) network, which provides capacity-building support via a trained clinical research nutritionist.

Emerging priorities

➔ The LEI Team's work plan and projected outcomes align closely with IARC's emerging priorities for 2021-2025, specifically in the areas of **evolving cancer risk factors and populations in transition**, as well as **implementation research**.

Main challenges

- **Funding constraints:** The Team leader is funded entirely by external funding.
- **Global competition for grants:** Increased competition for available grant funding on a global scale.
- **Data availability:** Challenges related to obtaining data for environmental impact analyses.
- **Administrative delays:** Issues with delays in administrative procedures.

Next steps

➔ **Explore understudied lifestyle behaviours**: Further research into understudied lifestyle behaviour areas, while considering the potential direct and indirect roles of stress in cancer development.

➔ **Enhance databases**: Improve cohort databases by incorporating high-quality planetary health indicators to investigate the co-benefits of healthy lifestyles for both human and planetary health.

RECOMMENDATIONS

The LEI Team is encouraged to:

✓ **Enhance collaboration across Branches**: Include team members from other branches (ENV, EPR, ESC/IMO) and consider appointing a co-leader from a different branch. Involve leaders or members of the Onco-Metabolomics (OMB) Team led by Dr Mazda Jenab and Dr Pekka Keski-Rahkonen (NME) to leverage expertise in biomarkers.

✓ **Foster synergies with other Teams**: Explore closer collaboration between the IEL team and the Nutrition, Cancer and Multimorbidity Team (NCM) led by Dr Heinz Freisling (NME).

✓ **Consider renaming the Team**: Rename the team to the "One Health" Team to reinforce the collaboration with ENV.

✓ **Strengthen cooperation with the *IARC Monographs* programme**: Align dietary research development with the high-priority recommendations list for 2025-2029.

Key publications

- Ladas EJ, Gunter M, Huybrechts I, Barr R. A Global Strategy for Building Clinical Capacity and Advancing Research in the Context of Malnutrition and Cancer in Children within Low- and Middle-Income Countries. J Natl Cancer Inst Monogr. 2019 Sep 1;2019(54):149-151. PMID: 31532534.

- Van Puyvelde H, Perez-Cornago A, Casagrande C, Nicolas G, Versele V, Skeie G, et al. (2020). Comparing calculated nutrient intakes using different food composition databases: results from the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort. Nutrients. 12(10):E2906.
- Huybrechts I, Jacobs I, Aglago EK, Yammine S, … Chajès V. Associations between Fatty Acid Intakes and Plasma Phospholipid Fatty Acid Concentrations in the European Prospective Investigation into Cancer and Nutrition. Nutrients. 2023 Aug 23;15(17):3695. PMID: 37686727; PMCID: PMC10489906.
- Huybrechts I, Rauber F, Nicolas G, Casagrande C, … Levy RB. Characterization of the degree of food processing in the European Prospective Investigation into Cancer and Nutrition: Application of the Nova classification and validation using selected biomarkers of food processing. Front Nutr. 2022 Dec 16;9:1035580. Erratum in: Front Nutr. 2023 May 16;10:1207555. PMID: 36590209; PMCID: PMC9800919.
- Hanley-Cook GT, Huybrechts I, Biessy C, Remans R, Kennedy G, Deschasaux-Tanguy M, et al. (2021). Food biodiversity and total and cause-specific mortality in 9 European countries: an analysis of a prospective cohort study. PLoS Med. 18(10):e1003834.
- Kliemann N, Rauber F, Bertazzi … Huybrechts I. Food processing and cancer risk in Europe: results from the prospective EPIC cohort study. Lancet Planet Health. 2023 Mar;7(3):e219-e232. Erratum in: Lancet Planet Health. 2023 May;7(5):e357. PMID: 36889863; PMCID: PMC10009757.
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- Huybrechts I, Kliemann N, Perol O, Cattey-Javouhey A, Benech N, Maire A, et al. (2021). Feasibility study to assess the impact of a lifestyle intervention during colorectal cancer screening in France. Nutrients. 13(11):3685.
- Ananyaa Mohan, Inge Huybrechts, Nathalie Michels. Psychosocial stress and cancer risk: A Narrative Review. Eur J Cancer Prev 2022

References

- Webpage of the LEI Team

Nutrition, Cancer and Multimorbidity (NCM) Team

Innovations Teams
➔ Starting date: January 2021

Members

Team leaders: Dr Heinz Freisling (Scientist, NME)

Team members: The NCM Team comprises 11 team members (3 scientists, 5 (+ 1 in October 2024, -1 left in Feb 2024) Early Career Scientists, 2 Visiting Scientists, 1 administrative assistant) from the NME Branch in Pillar 2.

➔ Scientists (NME): Dr Pietro Ferrari; Dr Vivian Viallon; Early Career Scientists (NME): Ms Emma Fontvieille; Mr Quan Gan; Ms Laia Peruchet Noray; Dr Anna Jansana (left 02/2024); Dr Alem Gebremariam (start 05/2024); Visiting Scientists (NME); Dr Reynalda Cordova; Dr Nazlisadat Seyed Khoei; Admin Assistant: Ms Karina Zaluski

Objectives

Context

- **Emergent health approach**: This approach recognizes that diseases should not be viewed as distinct entities; instead, they interact with one another and can exacerbate the negative health effects of shared risk factors.
- **Definition of multimorbidity**: Multimorbidity is defined a priori based on leading causes of death and potential concordance in etiology. Cardiovascular disease, type 2 diabetes, and cancer are among the leading causes of death that share several significant risk factors.
- **Key risk factors**: Obesity, physical activity, and diet are particularly relevant in the context of multimorbidity.

The NCM Team was established in 2021 with the following main objectives:

1. **Robust scientific evidence**: To provide solid scientific evidence regarding the roles of nutrition, obesity, physical activity, and metabolic dysfunction in the etiology of multimorbidity involving cancer and cardiometabolic diseases.
2. **Survival data**: To gather data on the impact of these factors on survival rates among individuals living with cancer.

The primary activities of the NCM Team include:

- **Cancer multimorbidity**:
  - Investigating the interplay between multimorbidity and cancer comorbidity.
- **Role of obesity and metabolic health**:
  - Understanding how obesity and metabolic health contribute to cancer development.
  - Identifying novel indicators of obesity and their relationship to cancer risk and survival.
- **Physical activity and sedentary behaviour**:
  - Strengthening the evidence for the roles of physical activity and sedentary behaviour in cancer risk and survival.

Workplan progress

Projects and consortia

The NCM Team actively contributes to various international projects, including:

- EPIC
- UK Biobank
- NCI Cohort Consortium

Applications and grants

Since its inception in 2021, the NCM Team has been involved in several funded projects supported by grants from organizations such as INCa and WCRF.

On multimorbidity:

- **Obesity and cancer risk:** Investigating the role of comorbidities in overall and cancer-specific mortality among patients with cancer (AdCoCanS-WCRF)
  - Duration: March 2020 – February 2024
  - IARC budget: £228 000 (€268 070)
  - Duration: December 2020 – November 2024
  - IARC budget: €118 553
- **Impact of pre-diagnostic obesity:** Examining the combined effects of pre-diagnostic obesity and comorbidities on prognosis and the risk of second primary cancer in cancer survivors (AdCoSurv-INCa)
- **Cancer risk from physical activity:** Assessing the relationship between physical activity, sedentary behaviour, and the role of cardiometabolic diseases and socio-economic position (CAPACITY-INCa)
  - Duration: December 2022 – December 2025
  - IARC budget: €110 378
    Duration: February 2022 – January 2026
  - IARC budget: £122 000 (€143 438)
- **Physical activity and cancer survival:** Investigating the combined impact of physical activity, sedentary behaviour, and cardiometabolic comorbidities on cancer risk and survival among cancer survivors (PaCoCanS-WCRF)
- **Lifestyle and cardiovascular disease:** Evaluating the impact of lifestyle and social inequality on fatal and non-fatal cardiovascular disease risk among cancer survivors (ILIAD-INCa)
  - Duration: December 2023 – December 2027
  - IARC budget: €210 187
- **Funding since 2021 on multimorbidity:** Total funding amounts to €850 626.
  - As coordinator: 3 grants
  - As co-applicant: 1 grant
  - As partner: 2 grants

Governance

Monthly meetings: The NCM Team convenes once a month to discuss relevant scientific topics, provide training and guidance to its members, and deliver administrative updates.

Reporting structure: The NCM Team leader regularly reports to the NME Branch Head, who offers guidance and suggestions regarding the Team's main activities and objectives.

Administrative support: Administrative guidance and support are provided by the NME secretaries.

On obesity and metabolic health:

- **Body shape phenotypes:** Investigating the relationship between composite body shape phenotypes of multiple anthropometric traits and the risk of cancer development (ShapeCancer-INCa)
  - Duration: November 2019 – November 2023
  - IARC budget: €137 791
- **Socioeconomic inequalities and cancer survival:** Examining the association between body shape phenotypes, socioeconomic inequalities, and cancer survival (SISCanS-INCa)
  - Duration: October 2022 – October 2025
  - IARC Budget: €204 587
- **Pre-diagnostic body shape phenotypes:** Evaluating survival and the risk of second primary cancer in cancer survivors based on pre-diagnostic body shape phenotypes (ShapeSurv-DFG)
  - Duration: May 2023 – October 2026
  - IARC budget: €63 630
- **Combined effects on metabolic markers:** Investigating the combined effect of pre-diagnostic body shape and physical activity by socioeconomic position on metabolic markers, cancer survival, and sequelae (BoSMile-INCa)
  - Duration: December 2023 – December 2026
  - IARC budget: €98 310
- **Diabetes and cancer:** Exploring links between diabetes and cancer using a multi-cohort analysis (DIACAN-INCa)
  - Duration: December 2021 – December 2025
  - IARC budget: €196 641

  - Note: The team leader took over this project after Dr Neil Murphy left the Agency.
- **Funding since 2021 on obesity and metabolic health:** Total funding amounting to €504 318.
  - As coordinator: 2 grants
  - As partner: 2 grants

Total funding (2021–2023)

- Total amount: €1 354 944
- Annual average: €451 648

Publications

See "Key publications" below for details.

Training

Dr Heinz Freisling leads the EPIC "Multimorbidity" working group and teaches at the IARC Summer School in Epidemiology, focusing on cohort study design.

Key collaborations

Cooperation across IARC Branches

The NCM Team includes staff from the NME Branch under Pillar 2. Although no collaboration with other branches is reflected in the Team's organizational chart, the NCM Team participates in projects involving other Branches, such as GEM, CSU, and EPR.

Collaboration with external partners

- **France**: **Centre Léon Bérard (CLB)**: B. Fervers; **"Exposome, Heredity, Cancer and Health" Team** at CESP U1018 Inserm: M. Kvaskoff and G. Severi
- **Austria**: University of Vienna: K.-H. Wagner and R. Cordova
- **Germany**: University of Regensburg: M. Leitzmann
- **Spain**: Idiap J. Gol: T. Duarte-Salle
- **United Kingdom**: University of Exeter: J. Bowden
- **Republic of Korea**: Seoul National University: A. Shin

Plans to expand the network to include partners from the USA (**NCI Cohort Consortium**) and Asia (**ACC**).

Main innovations

- **Multimorbidity research:** Studies focusing on the interplay between cancer and cardiometabolic diseases.
- **Cancer survival:** Investigating factors that influence survival rates in patients with cancer.
- **Obesity and metabolic health:** Understanding the roles of obesity and metabolic health in the development of cancer.
- **Obesity indicators:** Exploring indicators of obesity, including body shape phenotypes.
- **Life-course approach:** Using a life-course perspective to study health outcomes.
- **Chronoactivity:** Examining the relationship between circadian rhythms and health behaviours.

Contributions to MTS implementation

Fundamental priorities

The activities are in accordance with the IARC MTS for 2021–2025, specifically **Objective 2: "Understanding the causes of cancer"** (Sub-objective 2.1 in the IARC Project Tree).

Emerging priorities

The NCM Team's work plan and projected outcomes align with IARC's emerging priorities for 2021-2025, particularly in addressing **cancer inequalities (Emerging Priority C).**

Main challenges

- A significant challenge facing the Team is that core members, including the Team leader, are entirely **dependent on external funding**.

Next steps

- ➔ **Coordination of research projects:** Facilitate the implementation of thematically related active research projects focusing on cancer and cardiometabolic multimorbidity.
- ➔ **Dataset curation:** Curate the EPIC Multimorbidity dataset and a dedicated UK Biobank dataset and establish an NCI Cohort Consortium project.
- ➔ **Implementation active projects:** Launch active projects centered on obesity and metabolic health.

RECOMMENDATIONS

The NCM Team is encouraged to:

- ✓ **Enhance collaboration across Branches**: Include Team members from other branches to foster collaboration across the Agency, focusing on CSU for cancer inequalities; ENV for cancer survival; GEM for complementary research. Appoint a co-leader from a different branch. Involve leaders or members from the LEI Team, led by Dr Inge Huybrechts (nutrition, ultra-processed foods), and the Hormones and Metabolism (HorM) Team, led by Dr Sabina Rinaldi and Dr Laure Dossus (obesity, metabolic health, and cancer).
- ✓ **Explore synergies with LEI**: Investigate deeper collaborations between the NCM Team and the LEI Team, particularly in areas concerning nutrition, cancer, and multimorbidity.

Key publications

4 publications related to "Cancer Multimorbidity"

- Fontvieille E, ..., Freisling H. Body mass index and cancer risk among adults with and without cardiometabolic diseases: evidence from the EPIC and UK Biobank prospective cohort studies. BMC Medicine, 2023.
- Kohls M, Freisling H, ..., Arnold M. Impact of cumulative body mass index and cardiometabolic diseases on survival among patients with colorectal and breast cancer: a multi-center cohort study. BMC Medicine, 2022.
- Jansana A, ..., Freisling H. Impact of pre-existing metabolic diseases on metastatic cancer stage at diagnosis: a prospective multinational cohort study. Cancer Communications, 2024.
- Cordova R, ..., Huybrechts I, Freisling H. Consumption of ultra-processed foods and risk of multimorbidity of cancer and cardiometabolic diseases: a multinational cohort study. The Lancet Regional Health, 2023.

4 publications related to "obesity and metabolic health"

- Sedlmeier A , ..., Freisling H. Body shape phenotypes of multiple anthropometric traits and cancer risk: a multi-national cohort study. British Journal of Cancer, 2022.

- Recalde M, ..., Freisling H and Duarte-Salles T. Longitudinal body mass index and cancer risk: a cohort study of 2.6 million Catalan adults. Nature Communications, 2023.
- Stein M, ..., Freisling H, ..., Weber A. Association between circadian physical activity patterns and mortality in the UK Biobank . International Journal of Behavioural Nutrition and Physical Activity, 2023.
- Peruchet-Noray L, ...Freisling H.. Tissue-specific genetic variation suggests distinct molecular pathways between body shape phenotypes and colorectal cancer. Science Advances, 2024.

References

- Webpage of the NCM Team

Occupational Cancer Epidemiology (OCE) Team

Innovations Teams
➔ Starting date: 2022

Members

Team leaders: Dr Ann Olsson (ENV) and Dr Mary Schubauer-Berigan (ESC)

Team members: T he OCE Team comprises 11 Team members (6 scientists, 4 post-doctoral scientist, 1 research assistant) representing different Branches: CSU (Pillar 1), ENV (Pillar 3) and ESC (Pillar 4).

- ➔ Scientists: Dr Isabelle Soerjomataram (Deputy Branch Head, CSU); Dr Joachim Schüz (Branch Head, ENV); Mr Liacine Bouaoun (Statistician, ENV); Dr Florence Guida (Scientist, ENV); Dr Mary Schubauer-Berigan (Branch Head, ESC); Post-doctoral scientists: Dr Bayan Hosseini (Postdoctoral Scientist, ENV); Dr Joanne Kim (Postdoctoral Scientist, ENV); Dr Felix Onyije (Postdoctoral Scientist, ENV); Dr Wendy Agathe Bijoux (Postdoctoral Scientist); Research assistant: Ms Monika Moissonnier (Data Manager and Analyst, ENV)

Objectives

Context

Occupational cancers account for 5% of all cancer cases, 80% of mesotheliomas, and 20% of lung cancers. Occupational exposures are generally modifiable, making many occupational cancers preventable. There remain significant gaps in understanding the exposure-response relationships and the low-level effects of many occupational carcinogens. Reliable local exposure information is crucial for assessing the burden of occupational cancer and developing effective prevention strategies. Current data primarily originate from Europe and North America, and may not be applicable to other regions.

Occupational cancer epidemiology is essential for identifying and quantifying risks through both community-based and industry-based studies. International collaborations are vital for establishing large-scale studies on occupational exposures and associated risks. The interplay of mixed exposures, particularly the combined effects of tobacco smoking and lung carcinogens, is of significant interest.

The OCE Team aims to conduct global studies and synthesize evidence to prevent occupation-related cancers among workers and their families. The specific objectives include:

- ➔ **Identify occupational carcinogens**.
- ➔ **Characterize effects** of known and suspected carcinogens, including exposure-response relationships and joint effects with other exposures (e.g., tobacco smoking).
- ➔ **Estimate the cancer burden** due to occupational exposures using high-quality data and standardized methodologies.
- ➔ **Enhance the development** of exposure and risk assessment tools in LMICs, identifying carcinogenic hazards in these regions.
- ➔ **Encourage standardized data collection** through epidemiological studies and cancer registries.
- ➔ **Build capacity and facilitate knowledge exchange** in occupational cancer epidemiology, particularly in under-researched settings, through collaborations and internships.
- ➔ **Develop a long-term strategy** for occupational cancer research at IARC, including standardized operating procedures and adaptable recommendations for future studies.

Workplan progress

Projects and consortia

The OCE Team is involved in various significant programmes and projects, including:
- **IARC Monographs:** Identification of carcinogenic hazards to humans.

- **SYNERGY project:** Pooled analysis of case-control studies on joint effects of occupational carcinogens in lung cancer development.
- **AGRICOH project:** International consortium of agricultural cohort studies.
- **ASBEST CHRYSOTILE COHORT study:** Investigating occupational exposure to chrysotile in Russian miners and processing facility workers.
- **International Nuclear Workers Study (INWORKS):** Study on health effects of protracted low-dose external radiation exposure.
- **Pooled Uranium Miners Analysis (PUMA):** Collaborative study pooling cohorts of uranium miners.
- **Pooled international analyses** of cohorts exposed to styrene, titanium dioxide, lead
- **Multicentre international cohort study:** Focused on workers in the pulp and paper industry.
- **Parental occupational exposure:** Research related to childhood cancer.
- **Occupational exposures and testicular cancer:** Projects such as TESTIS-PRO and NORD-TEST.

Governance

No regular OCE meetings, but frequent project-specific meetings are conducted.

Collaboration with WHO
As per the IARC-WHO Standard Operating Procedure (SOP), WHO headquarters is informed of the results of the *IARC Monographs* evaluations. Establishing a direct liaison with WHO headquarters on occupational cancers is essential. Identifying focal points at WHO is necessary for effective collaboration.

On 26 September 2023, the OCE Team invited representatives from both the ILO and WHO to IARC. The identified WHO focal points present were Dr Ivan Ivanov (Occupational Health); Dr Frank Pega; Dr André Ilbawi (Cancer).

Applications and grants
Since 2022, the OCE Team has secured funding from:
- **Fondation de France**: €64 090.
- **INCa**: €139 509.

Total funding: €203 599.

A pending application for a project on night shift work is in the second stage, seeking €152 437.
Each project operates with its own funding, independent of the OCE's coordination.

Publications
See "Key publications" below.

Training
The OCE Team emphasizes training by providing training for postdoctoral students in occupational cancer epidemiology.

Main innovations

- **Epidemiological studies:** Focus on occupational cancer in LMICs.
- **Mixed exposures:** Investigations into the joint effects of mixed exposures on cancer risk.
- **Cancer burden estimation:** Estimation of the cancer burden attributable to occupational carcinogens.

Contributions to MTS implementation

Fundamental priorities
The OCE Team's work plan aligns with the IARC MTS 2021-2025, specifically:
- ➔ **Objective 2**: Understanding the causes of cancer.
- ➔ **Objective 4**: Synthesizing and mobilizing knowledge and strengthening global capacities in cancer science.

Key partners

Cooperations across IARC Branches
The OCE Team includes personnel from CSU, ENV, and ESC.

Collaboration with external partners
The Team contributes to international studies with different external partners (see "Projects and consortia" above).

Contributes to specific Level 3 objectives of the MTS:

- ➔ **2.1**: Enhancing understanding of new and known causes/risk factors for human cancer.
- ➔ **2.2**: Understanding exposure sources related to cancer disparities.
- ➔ **12.2**: Focusing on under-researched populations in LMICs.
- ➔ **4.4**: Evaluating emerging cancer hazards through expert assessments.

Main challenges

- **Consolidating expertise in implementation research** within the OCE Team.
- **Securing a larger number of international grants** with increased funding size.

Next steps

Continue studies in occupational cancer epidemiology to:

- ➔ Identify and characterize **occupational risks**.
- ➔ Develop a **long-term strategy** for occupational cancer research at IARC.
- ➔ Support **synthesis of evidence** for IARC Monographs evaluations.
- ➔ Estimate the **occupational cancer burden** (population attributable fraction, PAF).

RECOMMENDATIONS

The OCE Team is encouraged to:

- ✓ Strengthen organizational aspects: Implement regular meetings, action plans, and follow-up processes and consider hiring a project assistant for administrative support.
- ✓ Enhance interaction with the *IARC Monographs* programme to align research on occupational carcinogens with high-priority recommendations for 2025-2029.
- ✓ Foster cooperation with WHO and ILO to translate epidemiological data into actionable preventive strategies, focusing on shared expertise (e.g., asbestos, second-hand smoking).

Key publications (2022-2024)

- Turner MC, Straif K, Kogevinas M, Schubaeur-Berigan MK. Five decades of occupational cancer epidemiology. Scand J Work Environ Health, 2024.
- Schüz J, Kovalevskiy E, Olsson A, et al. Cancer mortality in chrysotile miners and millers, Russian Federation: main results (Asbest Chrysotile Cohort-Study). J Natl Cancer Inst 2024;
- Kreuzer M, Sommer M, Deffner V, Bertke S, Demers PA, Kelly-Reif K, et al. (2024). Lifetime excess absolute risk for lung cancer due to exposure to radon: results of the pooled uranium miners cohort study PUMA. Radiat Environ Biophys. PMID:38172372
- Xu M, Ho V, Lavoué J, Olsson A, Schüz J, Richardson L, et al. Prevalent occupational exposures and risk of lung cancer among women: Results from the application of the Canadian Job-Exposure Matrix (CANJEM) to a combined set of ten case-control studies. Am J Ind Med. 2024 Jan 8. PMID: 38192156.
- Ohlander J, Kromhout H, Vermeulen R, Portengen L, Kendzia B, Savary B, et al. Respirable crystalline silica and lung cancer in community-based studies: impact of job-exposure matrix specifications on exposure-response relationships. Scand J Work Environ Health. 2024 Jan 24:4140. PMID: 38264956.
- Wan W, Peters S, Portengen L, Olsson A, Schüz J, Ahrens W, et al. Occupational Benzene Exposure and Lung Cancer Risk: A Pooled Analysis of 14 Case-Control Studies. Am J Respir Crit Care Med. 2023 Oct 9. PMID: 37812782.

- Olsson A, Bouaoun L, Schüz J, et al. Lung Cancer Risks Associated with Occupational Exposure to Pairs of Five Lung Carcinogens: Results from a Pooled Analysis of Case-Control Studies (SYNERGY). Environ Health Perspect. 2024 Jan 18;132(1):17005. PMID: 38236172
- Leuraud K, Laurier D, Gillies M, Haylock R, Kelly-Reif K, Bertke S, Daniels RD, Thierry-Chef I, Moissonnier M, Kesminiene A, Schubauer-Berigan MK, Richardson DB. Leukemia and lymphoma mortality after low level exposure to ionizing radiation: Updated findings from an international cohort study of nuclear workers (INWORKS). 2024 Sept; Lancet Haematol.
- Guth M, Pilorget C, Lefevre M, Coste A, Danjou A, Dananché B, et al. TESTIS study group. Occupational exposure to organic solvents and the risk of developing testicular germ cell tumours (TESTIS study): Effect of combined exposure assessment on risk estimation. Scand J Work Environ Health. 2024 Apr 10:4161. PMID: 38597023.
- Paul A, Danjou AMN, Deygas F, Guth M, Coste A, Lefevre M, et al. Parental occupations at birth and risk of adult testicular germ cell tumours in offspring: a French nationwide case-control study. Front Public Health. 2024 Jan 16;11:1303998. PMID: 38292387.
- Richardson DB, Leuraud K, Laurier D, Gillies M, Haylock R, Kelly-Reif K, Bertke S, Daniels RD, Thierry-Chef I, Moissonnier M, Kesminiene A, Schubauer-Berigan MK. Site-specific cancer mortality after low level exposure to ionizing radiation: findings from an update of the International Nuclear Workers Study (INWORKS). Am J Epidemiol 2024 Aug
- Middleton DRS, Wedekind R, Hall AL, Suonio E, DeBono NL, Vermeulen RCH, Fritschi L, Stewart PA, Schubauer-Berigan MK. The development of exposure assessment critical reviews in carcinogenic hazard identification: the IARC Monographs experience. Occup Environ Med 2024 Aug
- Moirangthem R, Hosseini B, Patil A, George GS, Manjrekar A, Doibale P, et al. Occupations and the risk of buccal mucosa cancer in Indian men: A multi-centre case-control study. Cancer Epidemiol. 2024 Aug 16;92:102644. PMID: 39153274.
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References

- Webpage of the OCE Team

Onco-Metabolomics Team (OMB)

Innovations Teams
➔ Starting date: January 2021

Members

Team leaders: Dr Mazda Jenab (Scientist, NME) and Dr Pekka Keski-Rahkonen (Scientist, NME)

Team members: The OMB Team comprises 11 team members (1 scientist, 4 post-doctoral scientists, 3 research assistants, 1 administrative assistant) from the NME Branch in Pillar 2.

- ➔ Dr Chrysovalantou Chatziioannou (Scientist, NME) [from May 2024]; Dr Mira Merdas (postdoc, NME); Dr Jaye Marchiandi (postdoc, NME); Dr Felix Boekstegers (postdoc, NME); Dr Inma Buenosvinos (postdoc, NME); Ms Vanessa Neveu (Research Assistant); Ms Nivo Robinot (Research Assistant); Ms Agneta Kiss (Research Assistant); Ms Sarah Sherwood (Administrative Assistant)
- ➔ External members: 6 Pre-Graduate Trainees: Yuhan Zhang (China; remote); Julie Andersson (Denmark; 1 month); Adeline Fontvieille (Canada; 6 months); Lucia Dancero (Italy; 4 months); Paula Buritica (Columbia; 1 month); Blanca Sansalvador (Spain; 3 months); 2 Senior Visiting Scientists: Dr Marc Gunter (ICL, UK); Dr Hwayoung Noh (Centre Léon Bérard, Lyon)

Objectives

The OMB Team focuses on the relationship between metabolic dysfunction, metabolite perturbations, and cancer development across various anatomical sites. Metabolism is influenced by a range of factors, including dietary and lifestyle habits, environmental and endogenous exposures, obesity, and genetic predisposition. In addition, the composition and metabolic activity of the gut microbiome can be affected by modifiable exposures, which may, in turn, have impacts on cancer development. However, the underlying metabolic mechanisms that link these exposures to cancer remain largely unknown.

In this context, the primary aim of the OMB Team is to investigate the roles of nutritional exposures and the exposome, as well as metabolic perturbations in cancer development, through a molecular epidemiology approach.

Reasearch focus

The key research objectives of the OMB Team include:

- Exploring Cancer Etiology: Conceptualizing and implementing studies that integrate metabolic, nutritional, and cancer epidemiology.
- Assessing Exposures: Using biomarkers, such as food metabolomes and microbial exposomes, to evaluate exposures linked to cancer.
- Developing Methodologies: Creating new laboratory and bioinformatics-based methodologies to advance research in this area.

The workplan of the OMB Team is organized around four main themes/objectives:

1. Metabolic Perturbations: Investigating the roles of metabolic disruptions, dietary factors, the microbiome, and the exposome in the development of cancer.
2. Metabolite Variations: Exploring variations in metabolites associated with cancer development and the underlying metabolic mechanisms involved.
3. Novel Biomarkers: Identifying new biomarkers that reflect dietary, lifestyle, and environmental exposures related to cancer risk factors.
4. Metabolomics Laboratory: Operating, maintaining, and enhancing the NME Metabolomics Laboratory while developing and implementing new laboratory and bioinformatics methodologies and data management tools.

Workplan progress

Projects and consortia

The OMB Team coordinates or directly contributes to a variety of international projects currently underway, including:

- EPIC
- Finnish Birth Cohort
- Canadian Longitudinal Study on Aging
- CORSA
- MetaboCCC

Applications and grants

The OMB Team funds its activities through various active grants from NCI, JPI-Europe, and WCRF, including the following projects, which serve as key sources of external funding:

- **Hepato-FLAME and Metabo-BTC (HRB-Ireland, NCI; Dr Mazda Jenab; 2023-2025)**
  Aim: Conduct untargeted and targeted metabolomics analyses of hepatobiliary cancers and assess gut barrier functionality and bacterial serology.
  Budget: €170 480 (Hepato-FLAME); €9 900.
  Objectives: Identify metabolic perturbations and pathways, and assess the role of specific bacteria in the development of these cancers.
- **ePIDEMIc (JPI-Europe; Dr Mazda Jenab; 2021-2024)**
  Aim: Explore the associations and mechanisms of action between cancer, chronic disease risk, glycation products, and reactive dicarbonyl compounds.
  Budget: €249 519.96.
- **Ob-Elix (WCRF; Dr Chrysovalantou Chatziioannou, Dr Pekka Keski-Rahkonen 2024-2027)**
  Aim: Understand the mechanisms linking obesity to colorectal cancer risk through metabolomic profiling.
  Budget: €376 872.05; €25 406.00.
  Objectives:
  - Identify metabolites associated with obesity in EPIC.
  - Assess associations with colorectal cancer (CRC) and weight loss using intervention study data (bariatric surgery, metformin, lifestyle changes).
  - Triangulate and evaluate the causality of metabolite-cancer associations using Mendelian Randomization (MR) (GECCO).

Total funding (2021-2024): €832 177.

Upcoming grant applications:

Several major grant applications are currently in progress or planned for 2024:

- **ImmunoMET (ANR-FWF bilateral)**: Plasma antibody repertoires of the gut microbiome and colorectal cancer.
- **EndoSCCAPE (WCRF)**: Diet, nitrosamines, and oesophageal squamous cell carcinoma precursors in the African oesophageal cancer corridor.
- **Metabo-MASH (WCRF)**: Role of hepatic steatosis in colorectal cancer development and blood metabolomics profiling of colorectal adenomas.
- **AddiBUGS (ANR Pepr-SAMS)**: Metabolomics profiling of blood and faecal samples to explore mechanisms of alcohol and sugar addiction, with applications to colorectal and hepatocellular cancers.
- **Hepa-Thyroid (INCa PRTK 2024)**: Systemic and hepatic thyroid hormone metabolism in hepatobiliary cancer development.

Governance

The governance of the OMB Team is structured around:

- **Regular meetings:** Scheduled monthly meetings and ad hoc discussions focused on ongoing research projects, new ideas, brainstorming, and open dialogue regarding any challenges.
- **Weekly laboratory staff meetings:** Consistent gatherings to ensure alignment and communication among laboratory staff.

Key collaborations

Cooperation across IARC Branches

The OMB Team primarily includes staff from the NME Branch, in Pillar 2. Although the organizational chart does not explicitly reflect collaborations with other Branches, the OMB Team actively participates in projects related to:

- **GEM**: Collaboration on the Mutographs project and markers of early detection.
- **Training programmes**: The OMB Team leaders conduct training programmes independently, without support from the LCB Branch.

Collaboration with external partners

- **France**: Centre Léon Bérard (CLB): B. Fervers; "Exposome, Heredity, Cancer and Health" Team at CESP U1018 Inserm: M. Kvaskoff and G. Severi
- **Austria**: University of Vienna: K.-H. Wagner and R. Cordova
- **Germany**: University of Regensburg: M. Leitzmann
- **Spain**: Idiap J. Gol: T. Duarte-Salle
- **United Kingdom**: University of Exeter: J. Bowden
- **Republic of Korea**: Seoul National University: A. Shin

Future expansion: Plans to expand the network to include partners from the USA (NCI Cohort Consortium) and Asia (ACC).

Collaborative projects:
Direct funding has been secured for innovative projects closely aligned with the OMB Team's objectives:

- **Metabo-PANC study**: Plasma metabolomics of pancreatic cancer cases and controls (David Hughes, Ireland; Pavel Soucek, Czechia; Danieli Campa, Italy).
- **Metabo-CRC study**: Plasma metabolomics of early-onset colorectal cancer cases and controls (Sergi Castellvi, Spain).
- **LITONAS study**: Plasma and faecal metabolomics of NASH patients undergoing healthy diet intervention (Cosmin Voican, Gabriel Perlemuter, France).

Publications

In the period since its inception from 2021 to November 2024, the OMB Team members produced 86 scientific publications with an average impact factor (IF) of 8.84, with the highest IF being 50.5 (published in Nature). Out of these 86 papers, the OMB Team members were listed as first (or joint first) author in 8 papers, as senior (or joint senior) author in 6 papers, as first and senior (or joint) in 11 papers, and as writing group members (indicating a strong contribution) in 54 papers. The OMB Team members also produced 5 review and 2 commentary papers. The skewness coefficient of the IF values of these publications is 3.33, indicating a strong trend towards higher IF values. A list of 20 out of the 86 papers which are most significant representations of our work is provided at the end of the assessment.

Training

The OMB Team has facilitated various training initiatives, including:

- Training sessions for Early Career Scientists (currently four) and PhD candidates (currently six) within the OMB Team.
- An OMB Team online training course on untargeted metabolomics in cancer research, collaboratively implemented with colleagues from Imperial College London and Mount Sinai School of Medicine (17-21 January, 2022).
- Key lectures and involvement from OMB Team members in the ColoMARK Course on Colorectal Cancer Epidemiology (November 2023).
- Participation in the IARC Summer School and other training initiatives.
- Invited speakers at various training courses and seminar series.

Main innovations

The key innovations of the OMB Team focus on several critical areas:

- **Gut microbiome dysbiosis**:
  - Identification and application of microbiome-derived metabolomic biomarkers.
  - Identification of metabolomic biomarkers associated with gut microbiome alpha diversity.
  - Profiling plasma antibodies related to gut microbiome exposures.

- **Application of metabolomics in cancer development**:
  - Analyses of metabolic pathways and comparisons across various cancer sites.
  - Enhanced annotation of specific metabolites and metabolic pathways derived from untargeted metabolomics features.
- **Multi-omics analyses**:
  - Integration of metabolomics, proteomics, and genomics analyses within projects such as Eulat-ERADICATE-GBC, conducted by Dr Felix Boeckstegers within OMB.
- **Development of metabolomics methods**:
  - Innovative methodologies for analyzing different body compartments, such as stool samples and tumour tissues.

Contributions to MTS implementation

Fundamental priorities

The work programme of the OMB Team aligns seamlessly with the fundamental activities outlined in the MTS by:

➔ **Understanding the causes of cancer**:
  - Identifying nutritional, lifestyle, infectious, and genetic risk factors for cancer.
  - Elucidating mechanistic and causal pathways that connect specific risk factors to cancer.

➔ **Generating evidence for effective interventions**:
  - Modifying exposure to modifiable risk factors.
  - Fostering early diagnosis of common cancer types.

➔ **Enhancing global knowledge on cancer hazards and prevention**:
  - Contributing findings to *IARC Monographs, IARC Handbooks*, and international cancer prevention guidelines (e.g., WCRF and ECAC guidelines).

Main challenges

The OMB Team faces several challenges, including:

- **Reliance on external funding**: Dependence on external budget (EB) funding for operations.
- **Administrative support**: Insufficient administrative support to manage the heavy administrative load associated with tasks such as preparing Material Transfer Agreements (MTAs) and Institutional Ethics Committee (IEC) applications.
- **Biospecimen logistics**: Inefficient logistics for biospecimen handling, coupled with a significant administrative burden and compliance issues related to GDPR.

Next steps

The OMB Team outlines the following next steps for further development:

➔ **Incorporate expertise:** Bring in specialized expertise from within IARC, such as collaborating closely with Dr Jin Young Park on the META-GC project focused on gastric cancer.

➔ **Cement the Team's role:** Establish the Team as an expert metabolomics laboratory that contributes significantly to international epidemiological cancer research.

➔ **Innovative approaches:** Develop specialized methodologies for metabolomics data analysis, including generation, feature-finding, annotation, pathway/network analyses, and result interpretation.

This development aims to:

➔ Generate robust new knowledge regarding cancer risk factors and elucidate the metabolic mechanisms and pathways involved in cancer development.

➔ Enhance understanding of the gut microbiome's role, its composition, and metabolic activity in tumorigenesis.

RECOMMENDATIONS

The OMB Team is encouraged to:

- ✓ Involve Team members from other branches (GEM for the Mutographs project, EPR, IMO, and LCB) to enhance collaboration.
- ✓ Integrate relevant studies from the Metabolic Epidemiology Team (MET), led by Dr Neil Murphy, following discussions with the Branch Head.
- ✓ Explore the possibility of establishing a dedicated colorectal cancer team that combines current OMB projects with initiatives from various branches focused on colorectal cancer (CSU, GEM, EPR).
- ✓ Align metabolomics research development with the WHO high-priority recommendations for 2025-2029.

Publications

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References

- Webpage of the OMB Team

Population-Based Long-Term Surveillance (LTS) IARC-Japan Team

Members

Team leaders: Dr Norie Sawada (Senior Visiting Scientist, NME; Chief, Division of Cohort Research, National Cancer Center Institute for Cancer Control (NCCICC), Tokyo, Japan) and Dr Pietro Ferrari (Branch Head, NME).

Team members: The LTS Team comprises 4 IARC team members (2 scientists from CSU and 2 scientists from NME). The Team also includes scientists from the NCCICC, Tokyo, Japan: Dr Tomohiro Matsuda and Dr Rieko Kanehara. Dr Marc Gunter, former NME Branch Head now at the Imperial College London is part of the Team.

➔ Dr Isabelle Soerjomataram (Deputy Branch Head; CSU); Dr Hadrien Charvat (Scientist, CSU); Dr Inge Huybrechts (Scientist, NME); Dr Heinz Freisling (Scientist, NME)

Innovations Teams
➔ Starting date: 2022

Objectives

This inaugural International Team is jointly coordinated by IARC and the Japan National Cancer Center's Division of International Health Policy Research.

The primary aim of the LTS Team is to establish a long-term follow-up research platform focused on studying lifestyle factors before and after cancer diagnosis. The Team seeks to identify associations between these factors and cancer prognoses, survival, treatment outcomes, and quality of life (QOL) after diagnosis.

Specific objectives include:

- Gather evidence to support improved prognosis for cancer survivors.
- Identify associations between lifestyle risk factors and cancer diagnosis, prognosis, survival, treatment, and quality of life after diagnosis.
- Develop a research platform for cancer survivors using data from cancer registries.

The activities of the LTS Team primarily depend on two major cohorts managed by the collaborating institutions:

- European Prospective Investigation into Cancer and Nutrition (EPIC) cohort
- Japan Public Health Center-based Prospective Study (JPHC) cohort

Workplan progress

Projects and consortia

- **Building a platform for cancer survivors from cancer registries**:
  - Examining the feasibility of creating a platform through negotiations with relevant stakeholders.
  - Launching a pilot study focused on registering cancer survivors and collecting Patient-Reported Outcome Measures (PROM).
  - Gathering questionnaires on quality of life from cancer survivors.

- **Evaluating the association of pre- and post-diagnostic lifestyles**:
  - Analyzing differences in lifestyle before and after cancer diagnosis using existing cohorts (JPHC and EPIC).
  - Investigating the impact of lifestyle and dietary changes on the prognosis of colorectal cancer (CRC) survivors within the JPHC and EPIC studies.

Governance

Monthly LTS Team meetings:

- Administrative updates
- Team member presentations
- Discussion of grant applications (2023-2024)
- Information sharing

Key partners

Cooperations across IARC Branches
The LTS Team is led by the IARC NME Branch in collaboration with the Japan National Cancer Centre. Currently, the team collaborates with Pillar 1 (CSU), but does not include participants from Pillars 3 and 4. In addition, the team does not currently have ECVSs, such as PhD students or postdoctoral researchers.

Collaboration with external partners
The LTS Team collaborates with several external partners, including:

- **EPIC** (European Prospective Investigation into Cancer and Nutrition)
- **JPHC** (Japan Public Health Center-based Prospective Study)
- **Asia Cohort Consortium**
- **Pooling Project of Prospective Studies of Diet and Cancer (DCPP)**

  - Preparing and submitting a draft focused on the prognosis of lifestyle and dietary changes in colorectal cancer survivors from the JPHC and EPIC studies.
  - Including additional analyses for other cancer survivors.

- **Protocol development for long follow-up platform:**
  - Implementing a follow-up system for cancer survivors in select areas of the JPHC-NEXT study, based on findings from the pilot study in Project 1.
  - Discussing challenges and improvements identified during the pilot study.
  - Developing an integrated protocol for the long follow-up platform.

Applications and grants

- **Previous applications:** Applications to the World Cancer Research Fund (WCRF) have been rejected, and applications were submitted to the National Cancer Institute (NCI) and the National Institutes of Health (NIH).
- **Future plans:** A new application to WCRF is planned for the 2024-2025 funding cycle.

Main innovations

- **Development of a long-term cancer surveillance platform:** Focused on monitoring lifestyle factors before and after cancer diagnosis.
- **International collaboration:** The team leverages partnerships between IARC and the National Cancer Center (NCC) in Japan.

Contributions to MTS implementation

Fundamental priorities

The work plan of the LTS Team aligns with two fundamental priorities of the MTS 2021-2025:

➔ **Data for action:** Enhancing the understanding and utilization of data for effective cancer control.
➔ **Understanding the causes of cancer:** Investigating the factors that contribute to cancer incidence and outcomes.

Main challenges

- **Pilot study support:** The pilot study in Japan requires additional support from IARC, which is currently under discussion with CSU.
- **Grant acquisition:** The team has not secured any grants in the past two years, despite applications submitted to the World Cancer Research Fund (WCRF) and the National Institutes of Health (NIH). The team is encouraged to reassess and enhance its resource mobilization strategy.

Next steps

According to the LTS Team, the forthcoming steps for the development of the Research Team include:

- ➔ **Feasibility assessment:** Further evaluating the viability of conducting research on patients with cancer using data from cancer registries as part of the primary objective (Study 1).
- ➔ **Enhancing collaborations:** Expanding partnerships to explore new projects aimed at identifying novel factors influencing cancer prevention and survival. Key areas of focus include:
  - The balance of plant versus animal protein consumption.
  - The impact of ultra-processed foods, considering the differences between dietary sources in Japan and other HICs.
  - Incorporating biomarkers into research, although this aspect falls outside the current Team's scope.

RECOMMENDATIONS

- ✓ As a relatively new Team operating from two locations (France and Japan), optimal structure and organization have yet to be established.
- ✓ The team leader and co-leader should consider hosting ECVSs or facilitating exchanges between IARC and NCC Japan. They should also involve scientists from Pillar 3 (implementation research) within the Team.
- ✓ Discussions regarding the feasibility of building a research platform for cancer survivors using registry data should be confirmed with the CSU. The Team is encouraged to define a more focused research topic, such as colorectal cancer, based on data available from the Japanese cohorts.
- ✓ The Team should explore opportunities to build upon the G7 cancer initiative to enhance their projects.

References

- Web page of the LTS Team
- Web page of EPIC
- Web page of JPHC

Public Health Decision Science (PHDS) Team

Innovations Teams
➔ Starting date: November 2021

Members

Team leaders: Dr Iacopo Baussano, EPR Branch, IARC

Team members: The PHDS Team comprises 17 Team members, including 14 members in the EPR Branch (Pillar 3) and 1 member in the CSU Branch (Pillar 1).

➔ Dr Freddie Bray (Branch Head, CSU); Dr Indira Adhikari (Postdoctoral Scientist, EPR); Dr Partha Basu (Branch Head, EPR); Mr Maxime Bonjour (Doctoral Student, EPR); Mr Andrei Cividjian (Master's Student, EPR); Dr Gary Clifford (Deputy Branch Head, EPR); Dr Abrham Dagne (Postdoctoral Scientist, EPR); Ms Philippine Gason (Project Assistant, EPR); Mr Damien Georges (Senior Research Assistant, Data Management/Analysis, EPR); Dr Andrea Gini (Postdoctoral Scientist, EPR); Dr Alina Macacu (Consultant, EPR); Dr Irene Man (Scientist, EPR); Dr Jin Young Park (Scientist, EPR); Dr Mary Luz Rol (Scientist, EPR); Ms Vanessa Tenet (Senior Research Assistant, Data Management/Analysis, EPR); Dr Rachel Wittenauer (Postdoctoral Scientist, EPR).

Objectives

The primary objective of the PHDS Team is to enhance public health decision-making at both global and local levels by developing predictive models that combine high-quality empirical data with advanced algorithms. This initiative focuses on infectious-agent-related cancers, particularly human papillomavirus (HPV) and cervical cancer, in both HICs and LMICs. By simultaneously addressing both contexts, the Team aims to accelerate the transfer of knowledge and technology from high-resource to low-resource settings.

The PHDS Team is dedicated to creating an open-source modeling platform specifically designed to simulate the natural history and control of HPV infections and cervical cancer. This platform will feature a range of integrated models of varying complexity and flexibility, enabling the adaptation of public health projections to assess the expected impact of HPV vaccination and cervical cancer screening based on local data and specific needs. In parallel, the PHDS Team is conducting field studies to evaluate the actual impact of HPV vaccination on HPV prevalence in selected countries. The data collected from these studies will inform the modeling platform and help generate context-specific recommendations for cervical cancer control. These recommendations will not only benefit public health authorities in the respective countries but also serve as guidance for stakeholders in countries that are still developing their cervical cancer control measures.

Research focus

The PHDS Team focuses on three main research areas:

1. **High-quality data collection**:
   - Evaluating the effectiveness of HPV vaccination among young women in selected LMICs through initiatives such as IARC's/WHO International Coordination Centre for HPV vaccination effectiveness studies (CHRONOS).
   - Conducting an HPV prevalence baseline survey among women living with HIV in Zimbabwe.
   - Analyzing existing data from monitoring studies conducted in Bhutan, Rwanda, Armenia, Uganda, Laos, and Zimbabwe.
2. **Open-source modelling platform**:
   - Creating models to simulate HPV infection transmission and cervical cancer progression.
   - Developing a variety of algorithms with different levels of complexity and flexibility for each group of models.
   - Integrating all models into a modular platform to facilitate the production of context-specific projections.

- Providing estimates of the impact of HPV vaccination and screening at the local level, along with the costs and resources needed to implement context-responsive policies.

3. **Standardized health and economic assessment**:
   - Developing standardized procedures and quality monitoring tools for conducting urine-based HPV prevalence surveys across diverse settings.
   - Defining and testing protocols for context-specific cost-effectiveness analyses of HPV vaccination and cervical cancer screening.
   - Working with other organizations and institutes to create exportable tools that facilitate public health decision-making.

Governance

The PHDS Team conducts bi-weekly meetings, divided into two groups: data collection and modelling. These regular meetings serve to assess the status of research activities, align deliverables with IARC's MTS, and address upcoming public health needs related to cervical cancer elimination. A strategic meeting to integrate the quinquennial EPR strategy is scheduled for 18 June 2024, with the EPR Branch. In addition, a strategic meeting for the PHDS Team will occur in October 2024 to prepare for the EPR Branch review.

Collaboration with WHO

The Research Team actively engages in the activities of the WHO Cervical Cancer Elimination Initiative, including participation in the CCEI stakeholders meeting held in Cartagena, Colombia on 5-8 March 2024, where the PHDS Team leader was present.

Workplan progress

Applications and grants

Initial funding (Exhausted: €1.4 million):

- **CIHR-MathID**: Using mathematical modeling and health economics to evaluate and optimize infectious disease prevention strategies.
- **BMGF HPV ARMENIA**: Conducting a multi-cohort single-dose impact study on the HPV vaccine in Armenia.
- **CoHeahr**: Comparing health service interventions for the prevention of HPV-related cancers.
- **UTA-DCA**: Direct contribution agreement with UTA.
- **India Vaccine Trial**

Current funding (Ongoing: €5.6 million):

- **METHIS**: Context-specific modeling of HPV.
- **ProMetHeos**: PROgression ModEl of the HPV infection (VUMC/KI).
- **WHO-Impact**: Measuring the impact of HPV vaccine introduction.
- **BMGF CHRONOS**: HPV Vaccine Effectiveness Coordination Center.
- **EC-CvC CanScreen**
- **HPV FASTER IMPLEMENT**

Submitted grants (€130 000):

- **EMPOWER**: Enhancing measures for promoting HPV vaccination and early detection of cervical cancer among women with a migration background in Sweden and the Netherlands.
- **Cancer RADAR**: Mapping cancer inequalities by migration background in Europe.

Publications

See "Key publications" below.

Training

- The PHDS Team collaborates with the LCB Branch to develop training programmes, including those under the BMGF project.
- The Team regularly organizes the IARC training course on Statistical Practice in Epidemiology using R (SPE-R).

Key collaborations

Cooperation across IARC Branches
The PHDS Team, led by the EPR Branch in Pillar 3, collaborates with the CSU Branch in Pillar 1 and the LCB Branch in Pillar 4. This collaborative effort complements the global data produced by CSU, focusing on context-specific modelling and responsive solutions. The findings from field studies aid in defining relevant prevention policies tailored to local contexts, aligning with the concept of "local health" as a complement to "global health." Furthermore, the PHDS Team maintains close interactions with the IARC Cervical Cancer Elimination Initiative (CCEI) Team and the IARC Research for Implementation (RFI) Team.

Collaboration with external partners
In addition to its partnership with WHO, the Research Team collaborates with various EU-funded consortia and direct funding from the Bill & Melinda Gates Foundation (BMGF). Key scientific collaborations include:

- Amsterdam UMC, Netherlands
- Karolinska Institutet, Sweden
- Pirkanmaa Hospital District, Finland
- Institut Català D'Oncologia, Spain
- Sciensano, Belgium
- Ljubljana University, Slovenia
- AOU Città della Salute di Torino, Italy
- HPV Board, Antwerp, Belgium
- Coalition to Strengthen the HPV Immunization Community (CHIC) Council, Jhpiego, Baltimore, Maryland, USA
- Department of Immunization, Vaccines, and Biologicals, WHO, Geneva, Switzerland
- INCa, Brazil
- Ministries of Health in Bhutan, Rwanda, Laos, Zimbabwe, and Armenia
- National Cancer Center and Cancer Hospital, Chinese Academy of Medical Sciences
- Risk-Based Screening for Cervical Cancer (RISCC) Consortium

Future expansion: Plans to expand the network to include partners from the USA (NCI Cohort Consortium) and Asia (ACC).

Main innovations

- **Context-responsive approach**:
  - The PHDS Team has adopted a context-responsive strategy for cancer control, particularly in cervical cancer elimination. This approach is vital for adapting global recommendations to local specifics, opportunities, and constraints, ensuring that they meet the needs of local stakeholders responsible for implementing overarching guidelines.
  - For instance, in collaboration with the Brazilian National Cancer Institute (INCa), the PHDS Team played a crucial role in advising the Brazilian National Immunization Technical Advisory Groups (NITAG). By leveraging scientific evidence and IARC's model-based evaluations on single-dose, catch-up, and vaccine dose-reallocation policies, the team contributed to the decision to transition the local HPV vaccination programme to a single-dose schedule and initiate a catch-up campaign. A similar initiative is currently underway with the Bhutanese Ministry of Health.

- **Integration of data collection with advanced modelling techniques**:
  - To facilitate context-responsive and locally tailored policies, it is essential that models are informed by and adapted to high-quality local data. The PHDS Team is actively involved in both data collection and the development of advanced modelling techniques.
  - Historically, cost-effectiveness models for cancer prevention programmes were developed primarily for HICs. There is a pressing need to create relevant models for LMICs

and BRIC nations, which face significant indirect costs. This new approach will also address the financial toxicity of cancer—the economic burden and distress that cancer imposes on patients and their families.

Contributions to MTS implementation

Fundamental priorities

The work of the PHDS Team aligns directly with the fundamental priority 3, "From Understanding to Prevention," of the MTS 2021-2025, specifically addressing the following Level 3 objectives:

- ➔ **Objective 3.1** Enhance understanding of evidence-based interventions for cancer prevention and control to support their practical application, including efforts to reduce cancer disparities.
- ➔ **Objective 3.2** Enhance understanding of the efficacy and effectiveness of population-based interventions and cancer prevention programmes.

In addition, the activities of the PHDS Team significantly contribute to the **WHO Global Strategy to Accelerate the Elimination of Cervical Cancer**, which is identified as a priority in the MTS 2021-2025. This underscores IARC's commitment to supporting the implementation of this global strategy.

Main challenges

The Team leader has identified several challenges facing the PHDS Team:

- **Limited human resources** and **inadequate organizational structure** within the EPR Branch.
- **Difficulties in retaining outstanding collaborators** within IARC.

Next steps

The leader of the PHDS Team plans to enhance the integration of data collection with advanced modelling techniques, focusing on monitoring the population-level impact of HPV vaccination and cervical cancer screening. The following next steps are proposed:

- ➔ **Monitoring impact**: Implementing strategies to assess the population-level impact of HPV vaccination and cervical cancer screening as part of WHO's broader strategy for cervical cancer elimination at the local level.
- ➔ **Workflow adaptation**: Modifying the PHDS Team workflows to support this goal, making it a key component of the Branch's Quinquennial Vision, which will be assessed next year.
- ➔ **Expanding approach**: Designing the proposed methodologies to be applicable to other elimination/control initiatives for vaccine- and screening-preventable diseases.

RECOMMENDATIONS

The PHDS Team is dynamic, well structured, and organized, with the Team leader successfully securing numerous grants for innovative projects aligned with IARC's mission and the implementation of the WHO CCEI.

- ✓ The Team leader should consider expanding the successful model developed for HPV and cervical cancer to other infectious-agent-related cancers, such as Helicobacter pylori and gastric cancer.
- ✓ The PHDS Team should collaborate with the CSU Branch to define optimal methods for integrating their data into IARC's global resources, such as Globocan.

Key publications

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Risk Assessment and Early Detection (RED) Team

Innovations Teams
➔ Starting date: July 2021

Members

Team leaders: Dr Mattias Johansson and Dr Hilary Robbins, Genomic Epidemiology (GEM) Branch

Team members: The RED Team comprises 14 members from GEM, with 12 nationalities: 1 P3 scientist; 2 P2 scientists; 1 P1 project officer, 5 post-doctoral scientists, 1 data manager, 2 administrative assistants, 1 visiting scientist; and 1 MSc student.

- ➔ Ms Karine Alcala (Senior Research Assistant, Data Management/Analysis, GEM); Dr Shayma Alwaheidi (Project Officer, GEM); Dr Xiaoshuang Feng (Postdoctoral Scientist, GEM); Dr Aida Ferreiro (Scientist, GEM); Dr Justina Onwuka (Postdoctoral Scientist, GEM); Dr Mahdi Sheikh (Scientist, GEM); Ms Andreea Spanu (Project Assistant, GEM); Ms Hana Zahed (Doctoral Student, GEM); Ms Natalia Alves De Oliviera Vaz (Project Assistant, GEM); Dr Allison Domingues (Postdoctoral Scientist, GEM); Dr Ryan Langdon (Postdoctoral Scientist, GEM); Dr Saeed Nemati (Visiting Scientist, GEM); Dr Jifang Zhou (Visiting Scientist, GEM).

Objectives

The RED Team conducts translational epidemiological research that spans the entire spectrum from discovery to implementation. The primary ambition of the RED Team is to **lead impactful research aimed at significantly reducing the burden of cancer**. The Team envisions informing primary prevention by **enhancing the understanding of cancer risk and etiology, while also optimizing early detection strategies for secondary prevention**. The RED Team focuses on various cancer types, with a particular emphasis on lung cancer, kidney cancer, and cancers associated with human papillomavirus (HPV).

The RED Team collaborates with large international partnerships to investigate risk factors, develop risk prediction tools, and identify and evaluate early detection biomarkers. By leveraging diverse conceptual, design, and analytical approaches, the RED Team seeks conclusive answers to critical research questions, often using the extensive data resources generated by consortium studies. A specific objective is to **assess the significance of evolving risk factors in cancer etiology among populations undergoing transitions**, including factors such as opioid and tobacco use, as well as obesity. The RED Team achieves this through collaborative projects with investigators worldwide, using traditional observational methods and instrumental variable methods while leveraging large genomic studies.

Another goal is to **enhance methods for early cancer detection**. A key strategy in this area is improving cancer-specific risk assessment by integrating novel risk indicators, particularly biomarkers, and validating existing risk prediction tools across diverse populations. The guiding principle is to design studies that closely resemble the target population to directly support implementation studies of biomarkers for early cancer detection.

Workplan progress

Projects and consortia

All RED Team projects involve international collaborations, with many including the coordination of large consortia. Key networks identified by the RED Team include:

- Lung Cancer Cohort Consortium (LC3)
- International Lung Cancer Consortium (ILCCO)
- MetKid Consortium
- Integrative Cancer Epidemiology Programme (ICEP)
- HPV Cancer Cohort Consortium (HPVC3)
- Opioid Cohort Consortium (OPICO)

Applications and grants

The RED Team currently holds 11 active grants, highlighting several major successes:

- **INTEGRAL-AT**: US$3.3 million
- **LEAP**: US$2 million
- **OPICO U01**: US$3 million

The principal funders for the projects led by the RED Team include the United States National Cancer Institute (NCI), World Cancer Research Fund (WCRF), Institut national du Cancer in France (INCa), Cancer Research UK (CRUK), and Lung Cancer Research Foundation (LCRF). The RED Team has been highly successful in securing grants, ensuring the continuity of its activities for the next five years.

Project	PI	Funder	Period	Total amount	IARC amount
INTEGRAL-AT	M. Johansson	NCI U19	2023-2028	US$ 12 million	US$ 3.3 million
LEAP	H. Robbins	NCI R01	2022-2027	US$ 2 million	US$ 2 million
OPICO	M. Sheikh	INCA	2022-2026	US$ 560 000	US$ 560 000
LCS-France	H. Robbins	INCA	2020-2024	US$ 213 000	US$ 213 000
ICEP	M. Johansson	CRUK	2020-2025	£7 million	£750 000
OPICO U01	M. Sheikh	NCI R01	2024-2029	US$ 3 million	US$ 3 million

Key publications

Since 2021, the members of the RED Team contributed to 108 scientific publications, including 36 publications led by the Team as first and/or last author. Nearly half of the publications are related to lung cancer early detection. The other publications deal with HPV related cancer and early detection, opium and smoking cessation, as well as obesity and cancer (see "Key publications" below).

Training

Members of the RED Team have contributed to a variety of training and teaching activities, including:

- **Cancer genomic epidemiology course**: "Future Directions and Challenges: Personalized Risk Prediction and Prevention," given remotely at Chiang Mai University, Thailand, February 2024.
- **Cancer epidemiology course**: "Lung Cancer Screening," University of Kentucky, October 2023, virtual lecture.
- **IARC Summer School**: "Lung Cancer," Lyon, France, July 2023, virtual lecture.
- **Panelist**: "Careers in Global Health," NCI Career Development Seminar Series, United States National Cancer Institute, March 2023, virtual.
- **Webinar speaker**: "The Present and Future of Lung Cancer Screening," IARC-ESMO.
- **Teaching lecture**: "Effect Modification," IARC Summer School, May-June 2021, virtual.
- **Roundtable speaker**: "Careers Abroad," NCI Division of Cancer Epidemiology and Genetics Fellows' Symposium, September 2020, virtual.
- **Teaching lecture**: "30 Minutes for Prevention of Lung Cancer," IARC, Lyon, France, December 2019.
- **Teaching lecture**: "Lung Cancer Screening," CEESO International Educational Course in Lung Cancer, Moscow, Russian Federation, May 2019.
- **Virtual lecture**: "Future Directions and Challenges: Cancer Risk Factors," Cancer Genomic Epidemiology Workshop, Chiang Mai University, February 2024.
- **Virtual lecture**: "Tobacco and Lung Cancer," University of Kentucky, October 2023.
- **Virtual seminar**: "A Journey from Opium Research to the Opioid Cohort Consortium (OPICO)," Global Genomic Medicine Collaborative (G2MC).
- **Chair of symposium**: "We Need to Talk About Living with Kidney Cancer," World Kidney Cancer Day, IKCC, June 2023, virtual.

Governance

The RED Team meets every two weeks and holds weekly one-on-one meetings with supervisors. In addition, the RED Team organizes quarterly vision and progress meetings, along with retreats for strategy development and team building.

In addition, the team has developed several YouTube videos, including:

- **World No Tobacco Day**: "Why It's Never Too Late to Quit Smoking, Even After a Cancer Diagnosis!" IARC YouTube Channel, 2023.
- **Bladder Cancer Awareness Month**: "Promising Biomarkers," IARC YouTube Channel, 2022.
- **Quitting smoking after a lung cancer diagnosis**, IARC YouTube channel, 2021.

Key collaborations

Cooperation across IARC Branches
The RED Team primarily collaborates with scientists from the GEM Branch but also maintains close partnerships with other scientific Branches, particularly:

- **Pillar 1** – Cancer Surveillance Branch (CSU): Focus on risk-based prevention policy and attributable fractions analyses (Dr Isabelle Soerjomataram).
- **Pillar 2** – Genomic Epidemiology Branch (GEM): Involvement in polygenic risk scores, obesity mechanisms, never smokers, smoking cessation after cancer onset, and HPV serology; Nutrition and Metabolism Branch (NME): Conducting Olink analysis of proteins for lung cancer risk in the Q100 study (Dr Sabina Rinaldi) and within the EPIC cohort (Dr Pietro Ferrari).
- **Pillar 3** – Early Detection, Prevention, and Infections Branch (EPR): Assessment of screening performance in Belarus (Dr Andre Carvalho); Environment and Lifestyle Epidemiology Branch (ENV): Study of the epidemiology of oesophageal cancer in high-incidence regions (Dr Valerie McCormack).

Collaboration with external partners
The RED Team engages in significant scientific collaborations within large cohort consortia, including:

- **Lung Cancer Cohort Consortium (LC3):** Comprising 25 cohorts across North America, Europe, Asia, the Middle East, and Oceania.
- **International Lung Cancer Consortium (ILCCO):** Featuring more than 50 global partners.
- **Lung Early Proteins Project (LEAP**): Collaborating with institutions such as the National Cancer Institute, Fred Hutchinson Cancer Research Center, University of Pittsburgh, Brown University, St. Elizabeth Healthcare, Sinai Health in Toronto, and Istituto Tumori in Milan.
- **Integrative Cancer Epidemiology Programme (ICEP):** Partnering with the University of Exeter, University of Oxford, McGill University, University of Ioannina, and Quadram Institute.
- **Opioid Cohort Consortium (OPICO):** Involving the National Cancer Institute, Morgan State University, Fred Hutchinson Cancer Research Center, Wake Forest University, University of New South Wales, Australian National University, University of Sydney, Tehran University of Medical Sciences, and Paris Descartes University.

Main innovations

The RED Team has demonstrated its capacity to manage large international consortia and maintain a vast network of scientific and medical partners. With a strong track record in risk assessment, the team has developed significant expertise, particularly in **lung cancer research**.

In addition, the RED Team serves as a platform for **skill development within ECVSs**, providing mentorship and defining Individual Development Plans (IDPs) for team members. The ECVS staff are trained in grant writing, oral presentations, and grant pitches. Furthermore, each publication undergoes a thorough review process, with data checked by another Team member. This code review not only contributes to the learning process but also ensures the integrity of IARC's data and publications.

Contributions to MTS implementation

Fundamental priorities

- The RED Team aligns with the fundamental **priority 2 of the MTS 2021-2025: "Understanding the Causes."** Its activities contribute to molecular and genomic epidemiology studies, which are crucial for identifying biomarkers of cancer development and elucidating potential causal pathways. The Team investigates the roles of obesity and metabolic factors across multiple cancer types and examines the influence of opium and opioids on cancer onset. The Team aims to estimate how genetic and other biomarkers can enhance early cancer detection. In addition, the RED Team facilitates international consortia to gather sufficient sample sizes for informative genetic and genomic studies and explores the usability of datasets available in regional databases.

Emerging priorities

- In relation to the emerging priorities of the MTS 2021-2025, the RED Team conducts projects focused on cancer risks among populations in transition, including opioid use, tobacco use, and obesity. Consequently, the Team contributes to the implementation of **Emerging Priority A: "Evolving cancer risk factors and populations in transition".**
- Within the framework of the INTEGRAL project, the RED Team has also evaluated the acceptability of using biomarkers for screening eligibility, corresponding to **Emerging Priority B: "Implementation research".**
- Furthermore, the Team collaborated on a study assessing the cost-effectiveness and impact of lung cancer screening in France, with findings applied to the design of the French lung screening pilot programme. This work aligns with **Emerging Priority C: "Economic and societal impact of cancer."** Overall, the RED Team's research activities directly contribute to the MTS 2021-2025 at multiple levels, including Fundamental Priority 2 and Emerging Priorities A, B, and C.

Main challenges

Leveraging its strong expertise in risk assessment and early detection, the RED Team faces both opportunities and challenges in developing innovative research activities, including:

- **Advancing methodologies** for a significant improvement in multi-cancer risk assessment.
- Evaluating and implementing **multi-cancer early detection tests**.

Next steps

The leaders of the RED Team have identified the following next steps for the RED Team:

- **Rebranding:** Transition from "Integrative Epidemiology Team" (IET) to "Risk Assessment and Early Detection" (RED) Team.
- **Consolidation of expertise:** Strengthening competencies in biostatistics.
- **Biomarker development:** Contributing to the definition of biomarkers and criteria for lung cancer screening eligibility to better target high-risk individuals who are not currently included in screening programmes.

RECOMMENDATIONS

The members of the RED Team are encouraged to contribute to the following initiatives:

- ✓ Establishing an IARC Research Team focused on lung cancer.
- ✓ Engaging in discussions regarding patents for biomarkers.
- ✓ Securing resources for upcoming programmes on multi-cancer early detection and multi-cancer risk assessment.

Key publications

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- The International Lung Cancer Consortium (ILCCO)
- IHCC Educational Webinar Series #10: 'A Journey from Opium Research to the Opioid Cohort

Report: Assessing IARC's global reach

Objective

The previous bibliometric analysis has highlighted IARC's impact in terms of academic excellence and leadership in scientific projects focused on cancer prevention. To further enhance this analysis, we aim to assess IARC's global reach by examining its media presence and influence in policy documents. This analysis will help us understand the diverse audiences IARC's research is reaching, from policymakers to the general public.

IARC's media presence

The first step in evaluating IARC's global reach is to analyze its media presence, specifically the frequency with which IARC's research is cited across various media platforms.

Overview

To begin, we reviewed Altmetric data on media citations of IARC's research from 2021 to 2024.

- During this period, 1435 IARC research outputs were referenced across various media channels. In total, IARC was mentioned 65 911 times, with 50 900 mentions on social media platforms (primarily X, accounting for 99%, with other platforms including Facebook, Google+, and Reddit). There were also 14 670 mentions in the press and blogs and 341 mentions in other sources, such as YouTube. Mentions in policy documents were excluded from this analysis, because they are addressed in the next section using a more comprehensive database.

- Notably, IARC's media presence increased significantly between 2021 and 2024 compared with the previous MTS (2016–2020) period. Press mentions were 2.4-fold higher, with an average of 4347 press citations per year and 13 561 social media citations per year, compared with 1781 and 12 197, respectively, in the 2016–2020 period.

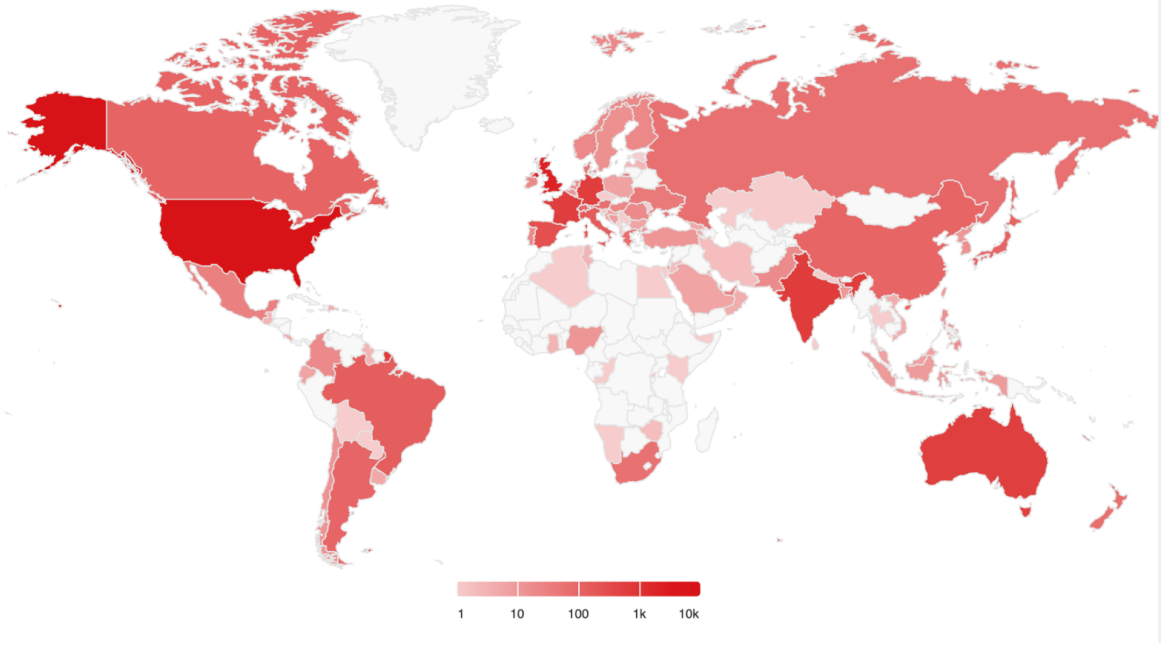
- In terms of geographical coverage, IARC's research was cited in 99 countries, including 45 LMICs in press mentions (**Map 1**). The Agency has the most media presence in the USA (53% of sources), the UK (14%), India (5%), Germany (4%), and France (4%). The most frequent citations came from *MSN* in the USA (297 citations), *MedicalXpress* in the UK (147 citations), The *Times of India* in India (36 citations), *Finanz Nachrichten* in Germany (93 citations), and *Le Monde* in France (95 citations). IARC also appeared in some of the most widely read newspapers in these countries, including one citation in *The New York Times*[28], two citations in BILD in Germany[29], and 47 citations in *The Guardian* in the UK.

[28] https://www.nytimes.com/2023/07/13/well/aspartame-sweetener-carcinogen.html

[29] https://www.bild.de/leben-wissen/wissenschaft/krebstod-mit-53-starb-der-super-size-me-star-durch-fast-food-6651ab69467fb867762f37f7; https://www.bild.de/ratgeber/2024/ratgeber/unaufhaltsamer-anstieg-bald-doppelt-so-viele-prostatakrebs-faelle-87797010.bild.html

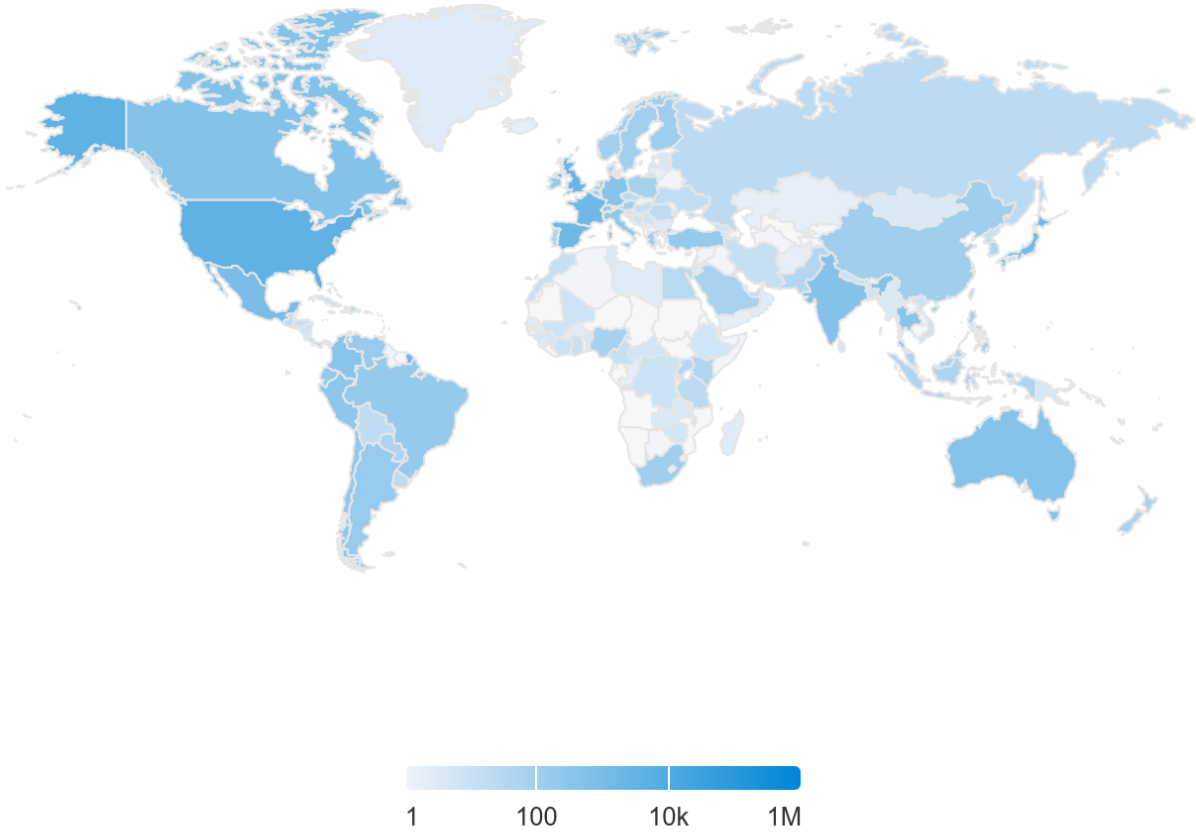
➔ The table below lists the top sources that have cited IARC at least 50 times during the 2021–2024 period.

Mention source	Country	# of mentions
MSN	USA	297
Yahoo! Finance	USA	232
Yahoo! News	USA	221
Cancer Cell International	United Kingdom	174
Yahoo!	USA	171
MedicalXpress	United Kingdom	147
Biospace	USA	141
MarketScreener	USA	130
Business Wire	USA	124
Morning Star	USA	113
Mirage News	Australia	108
Medscape	USA	106
Le Monde	France	95
Finanz Nachrichten	Germany	93
Health Reporter	USA	88
EurekAlert!	USA	87
The Medical News	Australia	85
Drugs.com	USA	84
Crwe World	USA	71
Newsbreak	USA	69
EX BULLETIN	USA	68
Doc Wire News	USA	67
ScienMag	United Kingdom	64
The Conversation	Australia	63
Medical News Today	United Kingdom	63
Spoke	USA	60
Stockwatch	USA	58
MedPage Today	USA	58
Nipponese.news	Japan	56
VB Profiles	USA	55
Nachrichten Welt	Germany	54
Le Lézard	France	54
PR Newswire	USA	53
LabRoots	USA	52
PharmiWeb	United Kingdom	51



Map 1. IARC in the press: distribution of mentions across 99 countries.[30]

➔ On social media, IARC was mentioned in 183 countries, including 80 LMICs (**Map 2**). Social media mentions have an increased activity from users in the USA (11%), UK (7%), Spain (5%), France (4%), and Japan (3%).



Map 2. IARC on social media: distribution of mentions across 183 countries.[31]

[30] Source: Altmetric.com
[31] Source : *Ibid.*

Most publicized research

The second phase of this analysis focused on identifying the IARC research outputs that garnered the most media attention. To do this, we used the Altmetric Attention Score, which tracks online engagement with research through various channels, such as news outlets, blogs, and social media. This score is weighted based on the influence of the source, with mentions in news articles carrying more weight than, for example, tweets. Although the Altmetric score highlights the level of public attention, it does not reflect the quality, scientific rigour, or long-term impact of the research. Trending topics or controversial issues can sometimes inflate the score, making it a less precise measure of a study's reliability. However, it remains a valuable tool for understanding how IARC's research is perceived and used by the media. In this exercise, we focus on research papers with an Altmetric Attention Score of at least 100, classifying them as highly influential. This score places these papers in the top 1% of all research articles in terms of media attention.

- We identified 118 articles with an Altmetric Attention Score of at least 100, indicating that 8% of IARC's research outputs that were cited in the media rank among the highest in terms of media exposure. Of these highly publicized papers, 18% were led by IARC, and 83% were open-access, underscoring the significant role open science plays in amplifying media coverage. A list of the 25 articles that achieved an exceptional Altmetric score, exceeding 1000, is provided in the annexes.

Most publicized Branches

A first analysis explores the media attention received by IARC publications, categorized by the organizational Branches. The focus is on both the number of papers that scored above 100 in the Altmetric Attention Score and the weighted attention scores. For example, papers with a score above 1000 carry significantly more weight in terms of media interest compared with those with a score of 200.

In parallel, some indicators on the media impact of the 10 IARC flagship programmes, which are key initiatives and are expected to have greater visibility within IARC's research portfolio, were collected. However, it is important to note that not all IARC flagship programmes receive significant media attention, because some are mechanisms with specific targets rather than research findings. For instance, the IARC Summer School does not involve direct research output, so its media presence is limited. Similarly, projects that primarily produce books, such as the IARC Handbooks and the WHO Blue Books, are likely to be under-represented because the Altmetric analysis primarily reflects media coverage of associated scientific publications.

- The NME Branch stands out as the most impactful in both citation volume and media engagement, highlighting the growing public interest in the links between lifestyle factors and cancer prevention (Figures 1 and 2). In addition, the work of CSU, and more broadly CSO 6: Cancer control, Survivorship and Outcomes research (Figure 3) also attracts significant media attention. Although CSU has fewer publications with an Altmetric score above 100 (N = 27) compared with NME (N = 50), the weighted media impact reveals that CSU's publications have a similar influence in terms of media coverage.

- The analysis of CSO areas receiving the most media attention reveals that it is not the specific Branch being publicized but rather the type of research produced. As illustrated in Figure 3, CSO 2: Etiology emerges as the area attracting the most attention. Research in this area from Branches other than NME, such as ENV's work on cellular telephone use and the risk of brain tumours, and exposure to ionizing radiation in workers, or ESC's studies on the carcinogenicity of substances such as aspartame, methyleugenol, isoeugenol, talc, and acrylonitrile, have also garnered significant media focus.

- CSO categories 1: Biology, 3: Prevention, and 4: Early Detection, Diagnosis and Prognosis, along with the IARC Branches working in these areas (EPR, EGM, and GEM), receive comparatively less media attention, probably due to the technical nature of the research in

these areas, which makes it more challenging to convey in simple terms to a general audience. These categories often focus on foundational or mechanistic aspects of cancer research, which, although crucial for scientific advancement, are less directly relatable to everyday life. As a result, they may not generate the same level of media interest as studies that have immediate implications for public health, prevention, or lifestyle changes, which are easier for the public to understand and engage with.

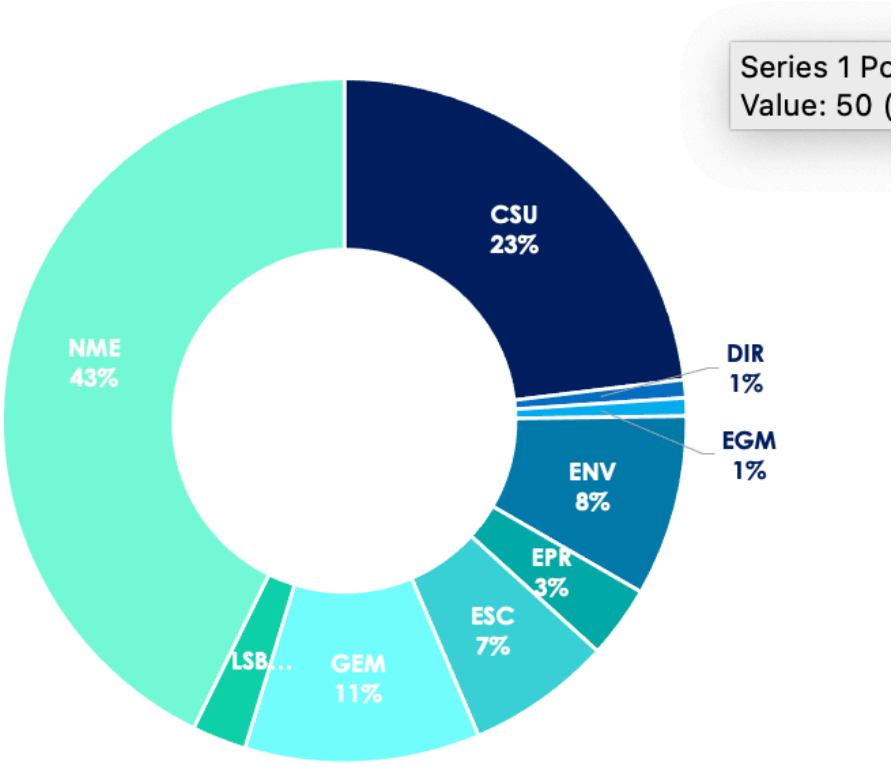


Figure 1. Distribution of IARC publications with Altmetric Score >100 by Branch.

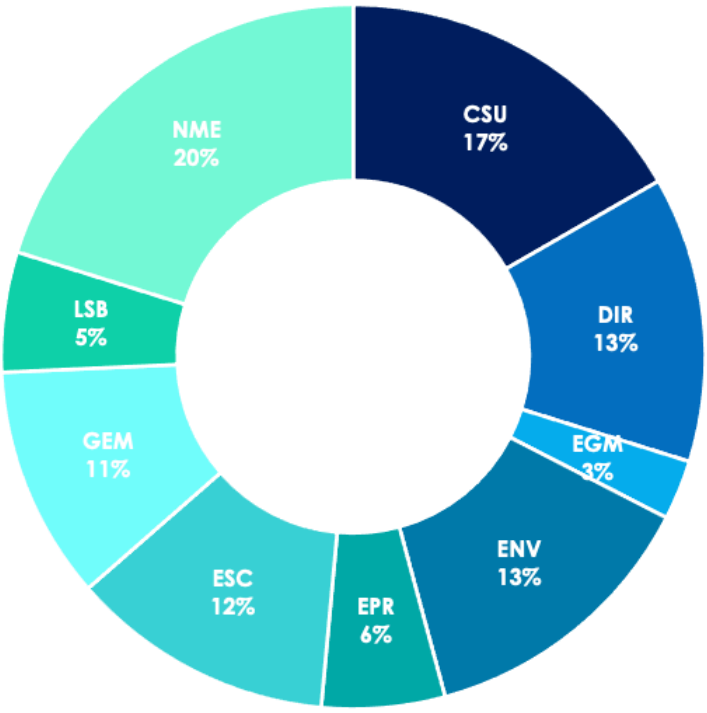


Figure 2. Weighted media impact by Branch based on Altmetric Score.

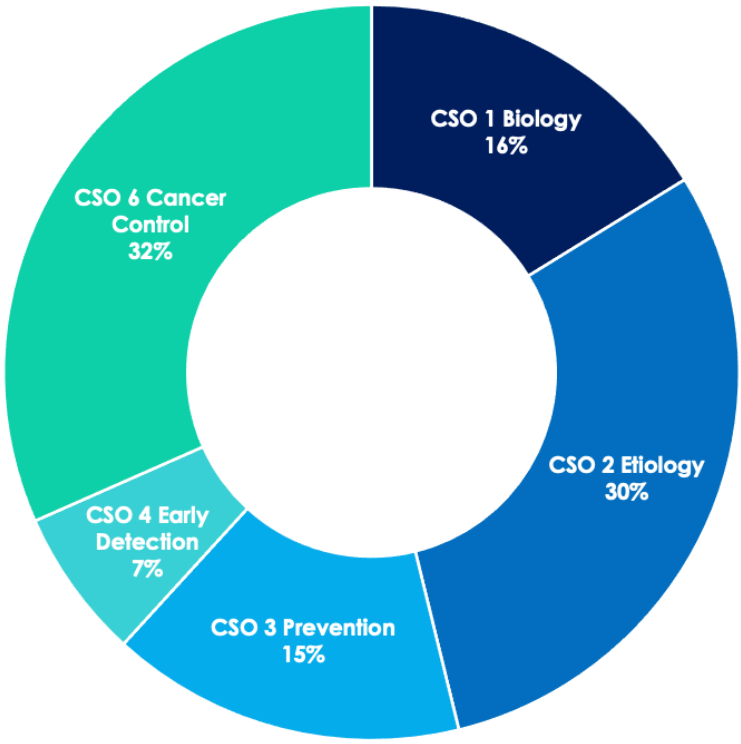


Figure 3. Weighted media impact by CSO area based on Altmetric Score.

➔ Among the IARC flagship programmes, GLOBOCAN stands out as the initiative with the most media attention. It achieved an impressive average attention score of 641, with 5 out of 9 publications scoring above 100. The project generated 5872 media mentions, with a significant proportion coming from the press (4086 mentions, compared with 1694

mentions for social media). GLOBOCAN's reach extended to 50 countries in press coverage and 75 countries in social media.

- EPIC also had high visibility, particularly on social media, but had a low attention score. The project had 1667 mentions (1413 on social media and 233 in the news), spanning 49 papers with an average attention score of 50. Four papers scored above 100 on the Altmetric scale. EPIC reached 25 countries through press coverage and 65 through social media.

- The World Code Against Cancer (through publications on the European Code and the Latin America and the Caribbean Code) faced more challenges in gaining media traction, despite efforts to enhance its visibility. Over the 2021–2024 period, 14 papers from the project were cited 427 times (10 mentions in the news and 416 on social media). However, the project had a relatively low reach, being cited in only 6 countries in the press and 28 on social media, resulting in a modest average attention score of 27.

The table below summarizes the media impact of IARC's main programmes, as measured by Altmetric scores. Publications have been categorized by programme based on keywords in their titles or abstracts. Consequently, some publications that belong to these programmes but do not contain the relevant keywords may be omitted, potentially underestimating the media impact of certain programmes.

IARC programmes	GLOBOCAN	EPIC	Code Against Cancer	Mutographs	CanScreen5	Monographs	Blue Books
IARC papers mentioned in media	9	49	14	1	2	5	13
Total media mentions	5872	1667	427	32	55	75	199
News mentions	4086	1413	10	1	5	71	193
Social media mentions	1694	233	416	31	50	3	4
Countries reached through social media	50	25	6	0	1	1	0
Countries reached through news	75	65	28	9	9	14	2
Average Altmetric Attention Score	641	50	27	26	21	10	10

Most publicized cancer sites

A second analysis provides a cross-cutting view of the media attention received by IARC's research outputs, classified by cancer site. By considering both the number of citations with an Altmetric Attention Score greater than 100 and the weighted attention score, we can identify patterns in public and media engagement with different types of cancer research.

- **Breast cancer**: Despite having only two publications cited (**Figure 4**), breast cancer research stands out with a significant weighted attention score of 814. This indicates that although the volume of publications is small, the individual studies generated considerable media and public interest (**Figure 5**). This may be driven by the relevance of breast cancer in global health conversations and the high profile of certain studies.

- **Other diseases**: Similar to breast cancer, research on other diseases related to cancer, such as type 2 diabetes or cardiovascular diseases, garnered only 15 citations (**Figure 4**) but achieved the highest attention score of 850 (**Figure 5**). This suggests that IARC's studies on

broader health issues outside oncology – potentially intersecting with major public health concerns – captured a significant share of media attention despite being less frequent.

- **HPV-Related Cancers**: Although cited only 3 times (**Figure 4**), HPV-related research achieved a moderate attention score of 358. The connection between HPV and cancer prevention efforts, particularly through vaccination campaigns, keeps this topic relevant, although it has not generated the same level of media attention as other areas.

- **Paediatric Cancer**: With just one citation (**Figure 4**) and a low attention score of 150 (**Figure 5**), paediatric cancer research remains a niche area in this dataset. Although it is of critical importance, it appears to have attracted limited media focus compared with adult cancer types.

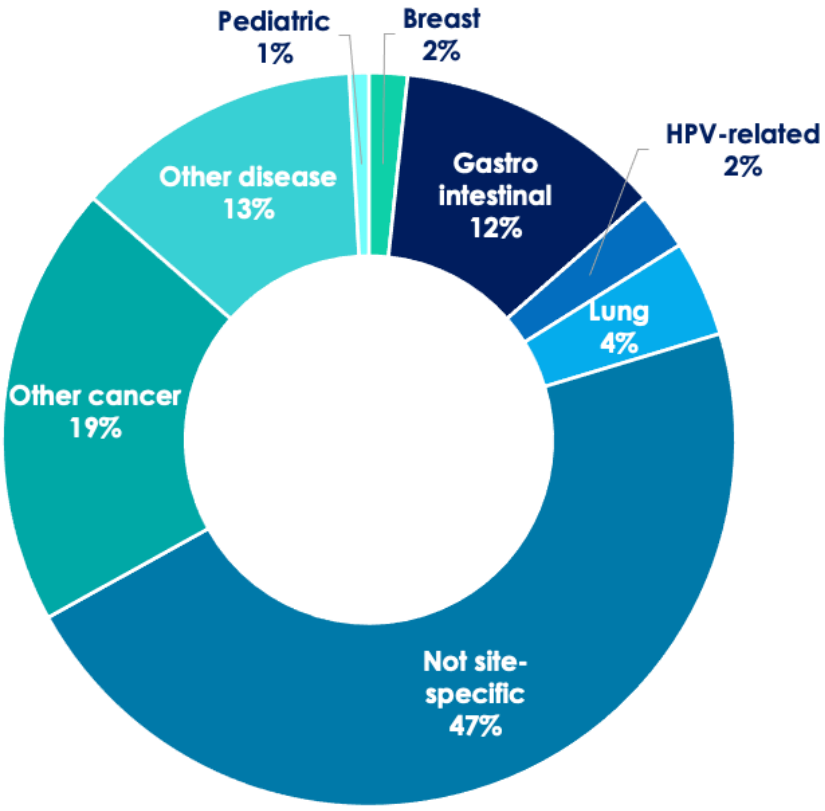


Figure 4. Distribution of IARC publications with Altmetric Score >100 by cancer site.

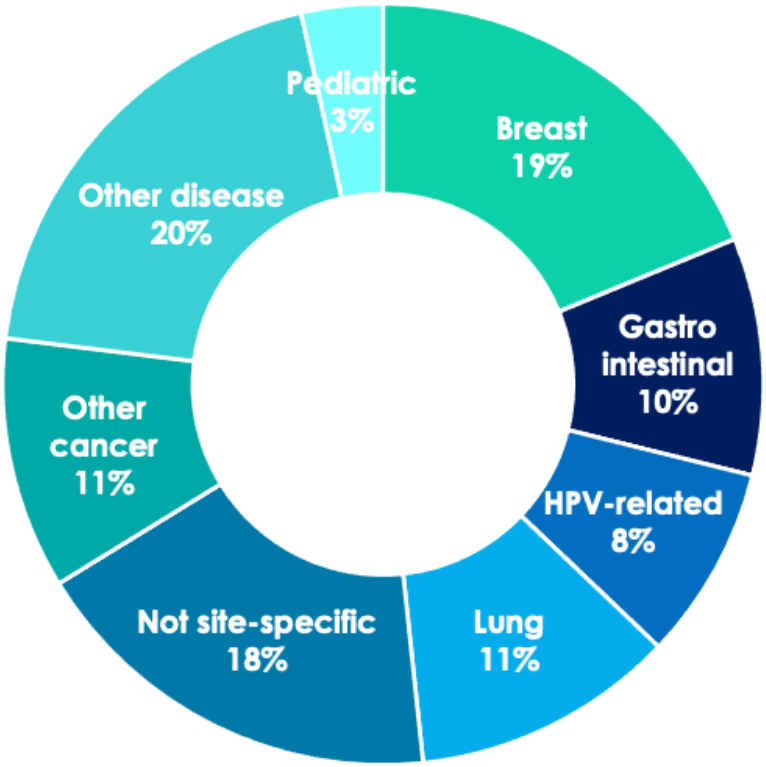


Figure 5. Weighted media impact by cancer site based on Altmetric Score.

IARC's impact in policy documents

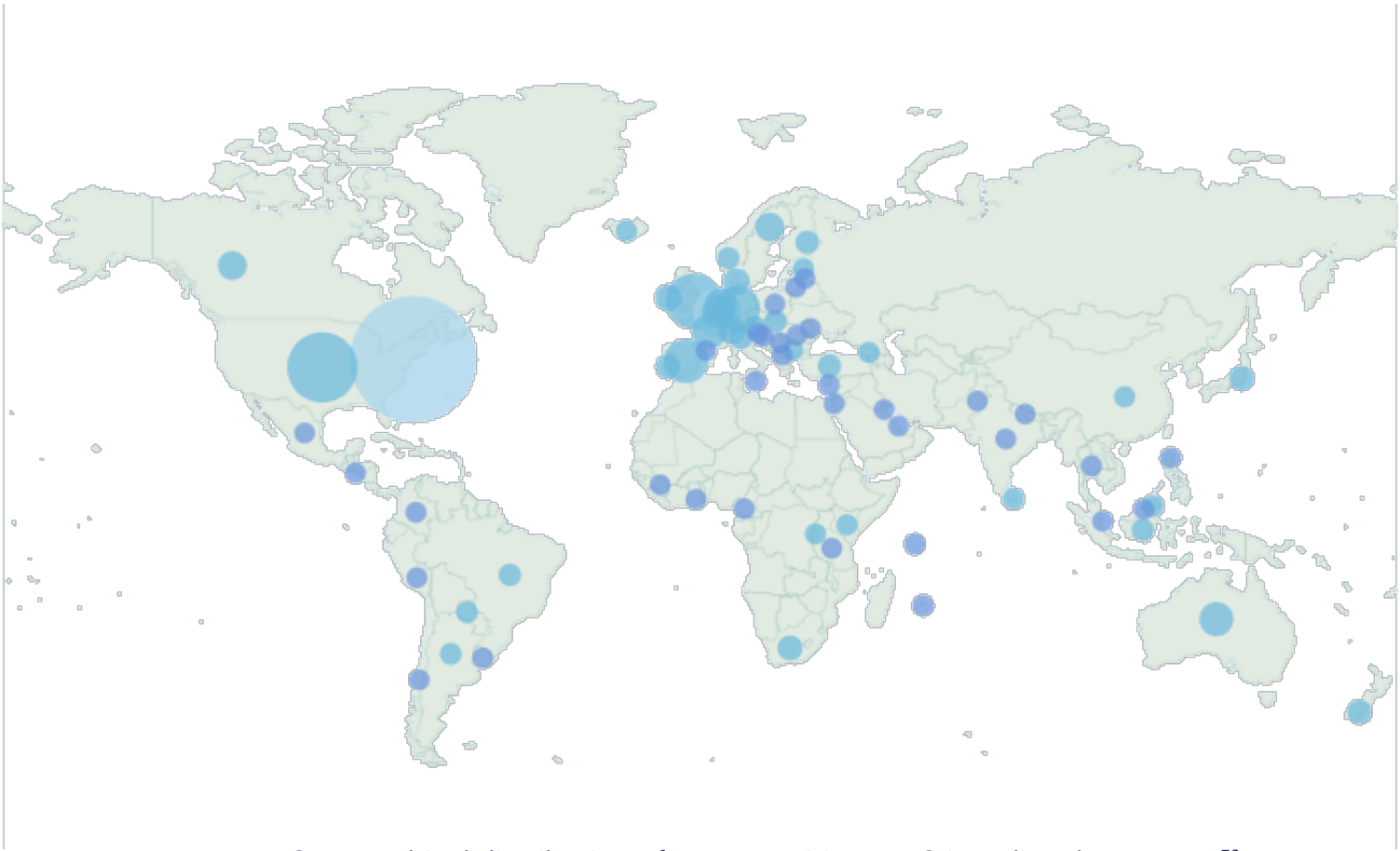
To complement the media analysis, we conducted an assessment of the impact of IARC's research on policy-making, a major aspect of its influence. For this analysis, we used the Overton database, a comprehensive platform that tracks the citation of research outputs in policy documents from governments, NGOs, and think tanks worldwide. By capturing how academic research informs public policy, Overton allows us to assess the real-world impact of scientific findings on decision-making processes.

Overview

For this analysis, we focused on policy documents citing IARC research and published in 2021–2024. Given the often-long timeframe for research to influence policy, we did not limit the analysis to publications released solely during the MTS period (2021–2024). We observed that many recent policy documents referencing IARC research often cite older publications. Thus, evaluating recent initiatives such as Mutographs or the LAC Code would not provide a full picture of their potential impact, which may take decades to materialize. At the conclusion of this exercise, we also include a list of the 10 most-cited IARC publications from 2021–2024 in policy documents to date, offering a snapshot of how recent work is beginning to influence policy discussions.

A total of 1403 publications from IARC were cited in 1915 policy documents. Most of these documents are standard publications (1541), followed by clinical guidance documents (324), indicating IARC's strong influence on shaping practical health recommendations and public policy.

IARC's influence spans numerous countries, with its research being cited in up to 72 countries by 303 different sources (**Map 3**).



Map 3. Geographical distribution of sources citing IARC in policy documents.[32]

[32] Darker bubbles represent counts = 1, while the larger, lighter bubble represents IGOs.

Governmental organizations account for 60% of the sources. However, LMICs make up only 6% of the total documents cited by governmental sources. This may be attributed to challenges in implementing research in LMICs, as well as structural differences in public health systems in LMICs, which often have fewer governmental agencies compared with HICs. Participating States contribute 59% of the total documents cited by governmental sources referencing IARC. However, Overton does not track citations translated into other languages, potentially under-representing countries such as the Russian Federation, China, and Japan.

Intergovernmental organizations (IGOs) make up 28% of the sources, with WHO citing IARC in 319 different documents and the European Union (EU) citing IARC in 136 documents.

Think tanks represent 10% of the total sources.

We then categorized the sources by type for a clearer understanding of how different organizations cite IARC's research:

Government > agency	121
Government > city	12
Government > food and drug safety	26
Government > healthcare agency	238
Government > legislation	3
Government > legislative research	14
Government > research center	22
Government > technology assessment	3
Government > transcripts	1
Igo > development bank	35
Igo > healthcare agency	297
Other > clinical guidelines aggregator	105
Think tank > agency	3
Think tank > consultancy	1
Think tank > industry association	12
Think tank > research center	21
Think tank > research centre	2
Think tank > university affiliated	27

Below is the list of IARC key sources, representing organizations that have cited IARC in at least 10 different policy documents during the 2021-2025 MTS period:

Intergovernmental organizations (IGOs):

- World Health Organization, Switzerland
- Publications Office of the European Union, Luxembourg
- United Nations, USA
- Pan American Health Organization (PAHO), USA
- World Bank, USA
- Organisation for Economic Co-operation and Development (OECD), France
- European Food Safety Authority (EFSA), Italy
- World Meteorological Organization, Switzerland
- Food and Agriculture Organization of the United Nations, Italy
- United Nations CEPAL, Chile
- Joint Research Centre, Italy
- European Parliament Committees, Belgium

Governmental organizations:

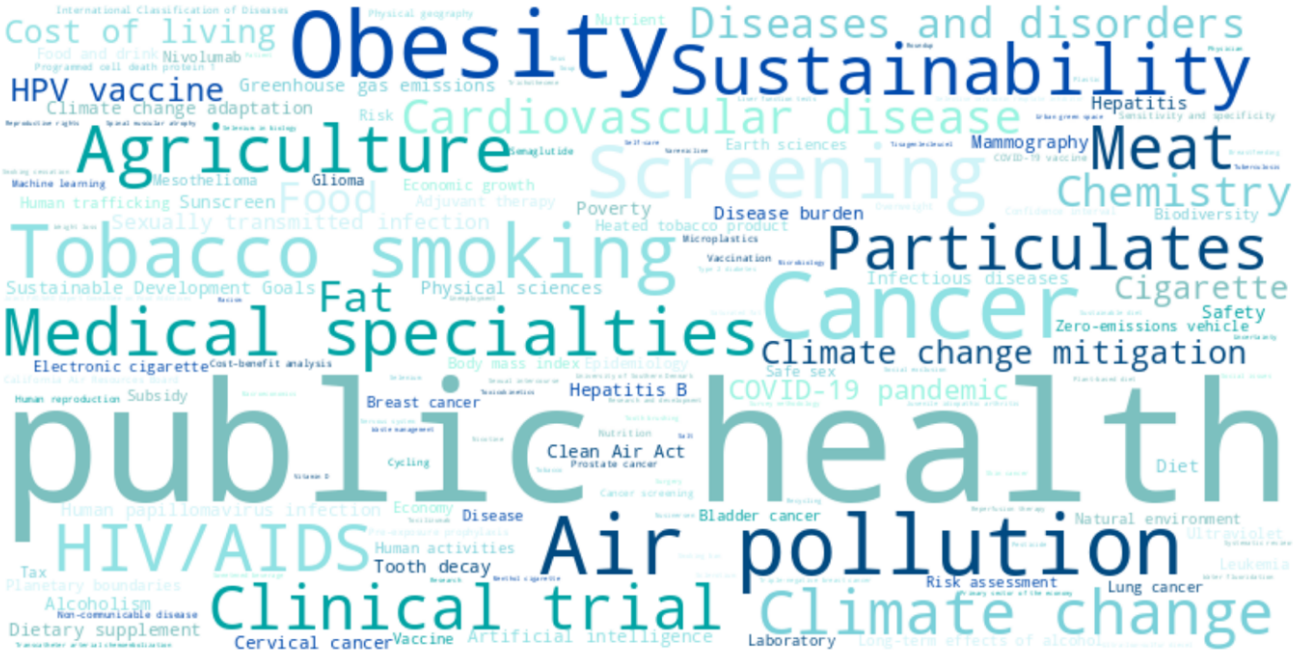
- Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF), Germany
- Generalitat de Catalunya, Spain
- UK Parliament Select Committee Publications, United Kingdom
- Belgian Federal Public Services, Belgium
- NICE, United Kingdom
- Government of Switzerland, Switzerland
- The UK Government, United Kingdom
- ANSES, France
- Centers for Disease Control and Prevention (CDC), USA
- Government of Japan, Japan
- Analysis and Policy Observatory, Australia
- Rijksinstituut voor Volksgezondheid en Milieu, Netherlands
- Federal Register, USA
- Strålsäkerhetsmyndigheten, Sweden
- Statens Institut for Folkesundhed, Denmark
- State of Texas, USA
- Umwelt Bundesamt, Germany
- Folketinget, Denmark
- Government of Italy, Italy
- Government of Portugal, Portugal
- Government of Türkiye, Türkiye
- State of California, USA
- Haute Autorité de Santé, France
- IZA Institute of Labor Economics, Germany
- National Cancer Registry Board, Ireland
- Santé Publique France, France
- Australian Institute of Health and Welfare, Australia
- Gezondheidsraad, Netherlands
- Government of Canada, Canada
- Government of South Africa, South Africa
- Comunidad Autónoma de la Región de Murcia, Spain

Other:

- Guidelines in PubMed Central, USA (clinical guidelines aggregator)

Key research areas

Unsurprisingly, IARC has significantly influenced public health policies. The most impactful policy documents – those frequently cited by other policy documents and thus having a greater impact on policy-making – cover key topics such as obesity, tobacco smoking, HIV/AIDS, the COVID-19 pandemic, the HPV vaccine, and screening. However, IARC's influence also extends to less-expected areas like agriculture, climate change, and poverty. To provide an overview of the topics covered by policy documents citing IARC's research, we have created the word cloud below.



Wordcloud of key topics of policy documents citing IARC.

In terms of IARC publications used in policy documents, these were classified by Common Scientific Outline (CSO) areas. The top areas were Etiology (46%), Cancer Control (41%), and Prevention (10%)—the latter mainly for work on the HPV vaccine. This mirrors the findings from the media coverage analysis.

Most of the research cited in policy documents relates to non-site-specific cancers (61%). However, two specific cancer types stand out in the top 100 IARC articles most cited in policy documents: cervical cancer (22%) and lung cancer (10%). The prominence of cervical cancer is expected, because IARC is a leading agency for the HPV vaccine, which has contributed to efforts towards elimination of HPV-related cancer. The notable presence of lung cancer, however, is somewhat surprising, because it is not traditionally one of IARC's top priorities, suggesting that it could potentially become a greater focus. Breast cancer represents only 4% of the research cited in policy documents.

IARC was the lead institution in 48% of the top 100 papers used in policy documents, underscoring its leadership and the recognition of its research excellence by policy-makers. This contrasts with media coverage, which tends to spotlight highly collaborative projects.

In addition, it is notable that 75% of the papers used in policy documents were published before 2015, and 30% were published before 2010, emphasizing the long-term impact of research on policy-making.

During this exercise, we also discovered that IARC had some unusual and unexpected impacts, such as being cited in the report *Mapping the Risk of Serious and Organised Crime Infiltrating Legitimate Businesses: Final Report*. This study, conducted by the Directorate-General for Migration and Home Affairs (European Commission), measures the economic and social harms of serious and organized crime. In this report, IARC's research from the *Pricing Policies and Control of Tobacco in Europe (PPACTE)* project was referenced, especially the *IARC Handbooks* Volume 14 on tobacco control.

Impact by Branch

Another analysis was conducted to assess the impact of IARC's scientific Branches on policy documents. To calculate the statistics for each Branch, the name of the Branch Head (including retired individuals) was used , because they are consistently cited in the publications representing the work of their entire team. Table 1 below offers a detailed overview of IARC's impact on policy documents, categorized by Branch, showcasing the number of articles cited, as well as the policy documents and sources referencing IARC research.

- CSU stands out with 179 articles cited in 485 policy documents, a significant contribution, particularly in publications (354) and clinical guidance (105). NME also plays a key role, contributing to 152 articles cited across 122 policy documents. Notably, GEM has a strong presence with 213 articles cited, but appears in fewer policy documents (71), suggesting that its impact may be more concentrated within specific domains.

- The majority of policy documents citing IARC research come from governmental organizations, particularly for branches such as GEM (76%) and NME (71%). IGOs such as the WHO and EU are significant sources, particularly for ESC (55%) and CSU (31%). The influence of think tanks is comparatively lower, but is still notable for branches like EPR (22%) and ESC (13%).

- Branches such as CSU and ESC have a strong international presence, with documents originating from 49 and 43 countries, respectively. However, the presence of IARC's work in LMICs remains modest overall (6%), with some branches, such as CSU (22%) and EPR (8%), having a stronger impact in these regions.

	IARC	CSU	GEM	LSB	NME	ENV	EGM	EPR	ESC
Article citations in policy documents:									
# of articles cited	1403	179	213	7	152	129	30	30	121
Types of policy documents citing IARC:									
# of documents	1915	485	71	18	122	104	30	52	432
- Publications	1541	354	54	14	103	92	28	45	347
- Clinical guidance	324	105	16	3	15	12	2	6	72
- Working papers	41	7	1	1	2	0	0	1	11
- Other[33]	9	19	0	0	2	0	0	0	2
Sources of policy documents:									
# of sources	303	129	32	10	58	51	15	22	126
% of docs from IGO	28%	31%	18%	44%	24%	27%	38%	34%	55%
- WHO docs	319	107	10	8	18	12	0	9	62
- EU docs	136	21	0	0	11	10	3	11	31
% of docs from gov.	60%	53%	76%	56%	71%	27%	59%	44%	32%
% of docs from think tanks	10%	9%	6%	0%	7%	7%	3%	22%	13%
Geographical reach:									
# of countries	72	49	15	6	22	22	9	11	43
% of docs from LMICs	6%	22%	3%	0%	4%	1%	0%	8%	4%

[33] Includes scholarly articles, white papers and blogs.

The following section presents a list of key sources for each IARC Branch, highlighting the organizations that most frequently cite their research. For each Branch, examples of one scientific publication integrated into a policy document are provided: one from an IGO and one from a governmental organization.

CSU:

Key sources citing CSU's research:

- United Nations
- World Bank
- Centers for Disease Control and Prevention (CDC)
- Pan American Health Organization (PAHO)
- United Nations Environment Programme (UNEP)
- Publications Office of the European Union
- Organisation for Economic Co-operation and Development (OECD)
- European Food Safety Authority (EFSA)

Example of international-level impact:

- **Publication cited**: *Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries*
  Freddie Bray et al. (2018)
  Published in *CA: A Cancer Journal for Clinicians*
- **Cited in**: *The State of the World's Children 2023*, UNICEF (April 19, 2023)
  This report was further cited in 23 policy documents.

Example of national-level impact:

- **Publication cited**: *Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries*
  Published in *CA: A Cancer Journal for Clinicians* (November 1, 2018)
- **Cited in**: This publication was cited 65 times by 31 sources across 17 countries between 2021 and 2024. One example is Japan's National Plan, *HPV Vaccine Fact Sheet Supplement*, Ministry of Health, Labour and Welfare, Government of Japan (March 13, 2024).

GEM:

Key sources citing GEM's research:

- United Nations
- Centers for Disease Control and Prevention (CDC)

Example of international-level impact:

- **Publication cited**: *Commentary: What can Mendelian randomization tell us about causes of cancer?*
  Daniela Mariosa et al. (2019)
  Published in *International Journal of Epidemiology*
- **Cited in**: *WHO European Regional Obesity Report 2022*, World Health Organization (May 2, 2022)
  - ➔ This report was further cited in *Current challenges and opportunities for addressing obesity*, Directorate-General for Internal Policies of the Union (European Parliament), Publications Office of the European Union (October 4, 2024).

Example of national-level impact:

- **Publication cited**: *Cigarette smoking and lung cancer—relative risk estimates for the major histological types from a pooled analysis of case-control studies*
  Beate Pesch et al. (2012)
  Published in *International Journal of Cancer*

- **cited in**: *Faisabilité de la mise en place d'un système de surveillance de l'incidence des cancers en lien avec l'activité professionnelle : étude pilote Sicapro (2010-2014)*
  Santé Publique France (August 20, 2021)

NME:

Key sources citing NME's research:
- United Nations
- World Bank
- Centers for Disease Control and Prevention (CDC)
- Pan American Health Organization (PAHO)
- Publications Office of the European Union
- Organisation for Economic Co-operation and Development (OECD)
- Food and Agriculture Organization of the United Nations (FAO)
- European Food Safety Authority (EFSA)

Example of international-level impact:
- **Publication cited**: *Glycemic index, glycemic load, and risk of coronary heart disease: a pan-European cohort study*
  Sabina Sieri et al. (2020)
  Published in *The American Journal of Clinical Nutrition*
- **Cited in**: *Tolerable upper intake level for dietary sugars*, EFSA (February 28, 2022) This publication was further cited in 40 other documents with national impact, including the *SACN report: Feeding young children aged 1 to 5 years*, Office for Health Improvement and Disparities, UK Government (July 4, 2023).

Example of national-level impact:
- **Publication cited**: *Lifestyle factors and risk of multimorbidity of cancer and cardiometabolic diseases: a multinational cohort study*
  Heinz Freisling et al. (2020)
  Published in *BMC Medicine*
- **Cited in**: *The burden of disease in Denmark - risk factors*, Statens Institut for Folkesundhed (February 28, 2023)

LSB:

Key sources citing LSB's research:
- World Bank
- Pan American Health Organization (PAHO)
- Organisation for Economic Co-operation and Development (OECD)

Example of International-Level Impact:
- **Publication cited**: *Editorial: Insights in coronavirus disease (COVID-19) - surveillance, prevention and treatment*
  Zisis Kozlakidis et al. (2022)
  Published in *Frontiers in Public Health*
- **Cited in**: *Guide to Adapting and Applying Evidence-Informed Guidelines. Second Edition*, Pan American Health Organization (PAHO) (July 21, 2023)

National-Level Impact:
- No citation at the national level found for the MTS period.

ENV:

Key sources citing ENV's research:
- United Nations

- United Nations Environment Programme (UNEP)
- Publications Office of the European Union
- Organisation for Economic Co-operation and Development (OECD)

Example of international-level impact:

- **Publication cited**: *European Code Against Cancer 4th Edition: 12 Ways to Reduce Your Cancer Risk*
  Joachim Schüz et al. (2015)
  Published in *Cancer Epidemiology*
- **Cited in**: *Beating Cancer Inequalities in the EU*, OECD (January 31, 2024)
  This publication was further cited in 15 policy documents.

Example of national-level impact:

- **Publication cited**: *Incidence and Mortality of Solid Cancers in People Exposed In Utero to Ionizing Radiation: Pooled Analyses of Two Cohorts from the Southern Urals, Russia*
  Alexander Akleyev et al. (2016)
  Published in *PLOS ONE*
- **Cited in**: *Nuclear Tests and Health: Consequences in French Polynesia*, La Documentation Française (February 24, 2021)

EGM:

Key sources citing EGM's research:

- United Nations Environment Programme (UNEP)
- Publications Office of the European Union
- Organisation for Economic Co-operation and Development (OECD)
- European Food Safety Authority (EFSA)

Example of international-level impact:

- **Publication cited:** Personalized early detection and prevention of breast cancer: ENVISION consensus statement
  Nora Pashayan et al. (2020)
  Published in Nature Reviews Clinical Oncology
- **Cited in:** Cancer Screening, SAPEA (February 25, 2022)
  - ➔ This publication was further cited in 8 policy documents and shaped the National Plan to fight cancer in Bulgaria, Ministry of Health, Government of Bulgaria (January 6, 2023).

Example of national-level impact:

- **Publication Cited:** Epigenetics as a mechanism linking developmental exposures to long-term toxicity
  R. Barouki et al. (2018)
  Published in Environment International
- **Cited in:** Rapport sur les causes d'infertilité (Report on the causes of infertility), La Documentation Française (February 18, 2022)

EPR:

Key sources citing EPR's research:

- United Nations
- World Bank
- Publications Office of the European Union
- Organisation for Economic Co-operation and Development (OECD)

Examples of national-level impact:

- **Publication cited**: *Can a single dose of human papillomavirus (HPV) vaccine prevent cervical cancer? Early findings from an Indian study*
  Rengaswamy Sankaranarayanan et al. (2018)
  Published in *Vaccine*
- **Cited in**: *Impact Evaluation of Australian National HPV Vaccination Program*, NCIRS (November 26, 2021)

Example of international-level impact:

- **Publication cited**: *Status of implementation and organization of cancer screening in the European Union Member States—Summary results from the second European screening report*
  Partha Basu et al. (2018)
  Published in *International Journal of Cancer*
- **Cited in**: *Cancer Screening*, SAPEA (February 25, 2022)
  - ➔ This publication was further cited in 8 policy documents, including the National Plan to fight cancer in the Republic of Bulgaria, Ministry of Health, Government of Bulgaria (January 6, 2023).

ESC:

Key sources citing ESC's research:

- United Nations
- World Bank
- Centers for Disease Control and Prevention (CDC)
- Pan American Health Organization (PAHO)
- United Nations Environment Programme (UNEP)
- Publications Office of the European Union
- Organisation for Economic Co-operation and Development (OECD)
- Food and Agriculture Organization of the United Nations (FAO)
- European Food Safety Authority (EFSA)

Note that *IARC Monographs* are counted as policy documents in Overton.

Example of international-level impact:

IARC Handbooks programme:

- **Publication cited**: *Bitumens and bitumen emissions, and some heterocyclic polycyclic aromatic hydrocarbons*
  Beatrice Lauby-Secretan et al. (2011)
  Published in *The Lancet Oncology*
- **Cited in**: *Review of Evidence on Health Aspects of Air Pollution: REVIHAAP Project: Technical Report*, World Health Organization (June 10, 2021)
  - ➔ This publication was cited by 347 other policy documents, including at national-level, e.g. *Methodological Manual for Air Pollution Health Risk Assessments in Switzerland*, Federal Office for the Environment, Government of Switzerland (November 14, 2023).

IARC Monographs programme:

- **Publication cited:** A Review of Human Carcinogens—Part D: Radiation
  Fatiha El Ghissassi et al. (2009)
  Published in *The Lancet Oncology*
- **Cited in:** Ozone and Ultraviolet Bulletin, Issue 2, World Meteorological Organization (October 10, 2024)

Examples of national-level impact:

IARC WCT:

- **Publication cited**: *The 2019 WHO Classification of Tumours of the Digestive System*
  Iris D. Nagtegaal et al. (2020)
  Published in *Histopathology*
- **Cited in**: *Robot-Assisted Versus Laparoscopic Distal Pancreatectomy in Patients with Resectable Pancreatic Cancer: An International, Retrospective, Cohort Study*, Generalitat de Catalunya (February 17, 2023)

Monographs:

- **Publication cited:** A Review of Human Carcinogens—Part F: Chemical Agents and Related Occupations Robert Baan et al. (2009) Published in The Lancet Oncology
- **Cited in:** *Avis relatif à la Prise en compte des facteurs nutritionnels et environnementaux via l'alimentation durant les 1000 premiers jours (c'est-à-dire entre la période péri-conceptionnelle jusqu'à l'âge de 2 ans) de la phase d'allaitement maternel en s'appuyant sur les derniers travaux de l'étude CONTA-LAIT Volet risques chimiques*, ANSES (September 14, 2024.

Annexes

List of the 25 articles that achieved an exceptional Altmetric score, exceeding 1000:

Title	Attention score	Branch	IARC lead
Artificial sweeteners and cancer risk: Results from the NutriNet-Santé population-based cohort study	4967	NME	No
Artificial sweeteners and risk of cardiovascular diseases: results from the prospective NutriNet-Santé cohort	4739	NME	No
Is early-onset cancer an emerging global epidemic? Current evidence and future implications	3985	NME	No
Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries	3479	CSU	No
Global burden of cancer in 2020 attributable to alcohol consumption: a population-based study	3290	CSU	No
Ultra-processed food consumption, cancer risk and cancer mortality: a large-scale prospective analysis within the UK Biobank	2669	NME	No
Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States, 2019	1917	CSU	No
Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries	1648	CSU	No
Longitudinal body mass index and cancer risk: a cohort study of 2.6 million Catalan adults	1472	NME	No
Association Between Childhood Consumption of Ultraprocessed Food and Adiposity Trajectories in the Avon Longitudinal Study of Parents and Children Birth Cohort	1419	NME	No
Postdiagnosis Smoking Cessation and Reduced Risk for Lung Cancer Progression and Mortality	1413	GEM	Yes
Identifying molecular mediators of the relationship between body mass index and endometrial cancer risk: a Mendelian randomization analysis	1398	NME	Yes
Accelerometer measured physical activity and the incidence of cardiovascular disease: Evidence from the UK Biobank cohort study	1367	GEM	Yes
Implications of food ultra-processing on cardiovascular risk considering plant origin foods: an analysis of the UK Biobank cohort	1342	NME	No
Consumption of ultra-processed foods and risk of multimorbidity of cancer and cardiometabolic diseases: a╪multinational cohort study	1316	NME	No
The 2021 WHO Classification of Tumours of the Central Nervous System: a summary	1237	ESC	No
Cellular Telephone Use and the Risk of Brain Tumours: Update of the UK Million Women Study	1230	ENV	Yes
International Pooled Analysis of Leisure-Time Physical Activity and Premenopausal Breast Cancer in Women From 19 Cohorts	1192	NME	No

Dietary exposure to nitrites and nitrates in association with type 2 diabetes risk: Results from the NutriNet-Santé population-based cohort study	1179	NME	No
Post-diagnosis adiposity, physical activity, sedentary behaviour, dietary factors, supplement use and colorectal cancer prognosis: Global Cancer Update Programme (CUP Global) summary of evidence grading	1173	NME	No
Global burden of primary liver cancer in 2020 and predictions to 2040	1136	CSU	Yes
Ultra-processed foods, adiposity and risk of head and neck cancer and oesophageal adenocarcinoma in the European Prospective Investigation into Cancer and Nutrition study: a mediation analysis	1134	NME	No
Coffee consumption is associated with a reduced risk of colorectal cancer recurrence and all-cause mortality	1126	NME	No
Cancer mortality after low dose exposure to ionising radiation in workers in France, the United Kingdom, and the United States (INWORKS): cohort study	1054	ENV	No

Top 10 most influential policy documents citing IARC, published in 2021-2024:

Title	Source Name	Source Country	Citations
Review of evidence on health aspects of air pollution: REVIHAAP project: technical report	World Health Organization	IGO	347
Urban green spaces and health	World Health Organization	IGO	126
Solar ultraviolet radiation: assessing the environmental burden of disease at national and local levels	World Health Organization	IGO	123
Economic cost of the health impact of air pollution in Europe: clean air, health and wealth	World Health Organization	IGO	121
Health at a Glance: Europe 2022	OECD	IGO	108
Mapping the risk of serious and organised crime infiltrating legitimate businesses: final report.	Publications Office of the European Union	EU	101
WHO European Regional Obesity Report 2022	World Health Organization	IGO	57
The report of the Commission on Race and Ethnic Disparities	The UK Government	UK	56
Safety evaluation of certain contaminants in food	Food and Agriculture Organization of the United Nations	IGO	51
2021 UNAIDS Global AIDS Update - Confronting inequalities — Lessons for pandemic responses from 40 years of AIDS	UNAIDS	IGO	40
Tolerable upper intake level for dietary sugars	EFSA	EU	40

Spreading like Wildfire: The Rising Threat of Extraordinary Landscape Fires - A Rapid Response Assessment	United Nations Environment Programme	IGO	40
Rural Development Report 2021	International Fund for Agricultural Development	IGO	38
Plates, pyramids and planet – Developments in national healthy and sustainable dietary guidelines: a state of play assessment	TABLE Debates	UK	35
Primary health care on the road to universal health coverage: 2019 global monitoring report	World Health Organization	IGO	34
100 Days Mission to Respond to Future Pandemic Threats	The UK Government	UK	33
Poverty and social exclusion in the WHO European Region: health systems respond	World Health Organization	IGO	31
Impact of economic crises on mental health	World Health Organization	IGO	31
Status report on alcohol consumption, harm and policy responses in 30 European countries 2019	World Health Organization	IGO	29
Tobacco: preventing uptake, promoting quitting and treating dependence	NICE	UK	28

Top 20 IARC publications cited in policy documents in 2021–2024 (including all IARC publications and those published during 2021–2024):

Title	Branch	# of citations	IARC lead
A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010	CSU	433	No
Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries	CSU	209	Yes
Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015	Multiple PI	158	No
Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012	CSU	133	Yes
Human papillomavirus is a necessary cause of invasive cervical cancer worldwide	Multiple PI	115	No
Carcinogenicity of consumption of red and processed meat	ESC	109	Yes
Cancer incidence and mortality patterns in Europe: Estimates for 40 countries in 2012	CSU	105	Yes
Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries	CSU	103	No
Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008	CSU	98	Yes
Global Cancer Statistics, 2002	CSU	95	Yes
Epidemiologic Classification of Human Papillomavirus Types Associated with Cervical Cancer	EPR	80	Yes

The carcinogenicity of outdoor air pollution	ESC	75	Yes
A review of human carcinogens—Part C: metals, arsenic, dusts, and fibres	ESC	74	Yes
Cancer survival in Australia, Canada, Denmark, Norway, Sweden, and the UK, 1995–2007 (the International Cancer Benchmarking Partnership): an analysis of population-based cancer registry data	ESC	72	No
Effectiveness of tax and price policies in tobacco control	ESC	71	No
Global cancer statistics	CSU	71	No
IPCS Conceptual Framework for Evaluating a Mode of Action for Chemical Carcinogenesis	ESC	70	No
Body Fatness and Cancer — Viewpoint of the IARC Working Group	ESC	69	Yes
The causal relation between human papillomavirus and cervical cancer	EPR	67	No
The relationship between different dimensions of alcohol use and the burden of disease-an update	CSU	64	No
2021-2024			
Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries	CSU	103	No
Global burden of cancer in 2020 attributable to alcohol consumption: a population-based study	Multiple PI	25	Yes
Association Between Childhood Consumption of Ultraprocessed Food and Adiposity Trajectories in the Avon Longitudinal Study of Parents and Children Birth Cohort	NME	12	No
The European cancer burden in 2020: Incidence and mortality estimates for 40 countries and 25 major cancers	CSU	10	No
Artificial sweeteners and cancer risk: Results from the NutriNet-Santé population-based cohort study	NME	10	No
Consumption of ultra-processed foods and risk of multimorbidity of cancer and cardiometabolic diseases: a multinational cohort study	NME	10	Yes
Artificial sweeteners and risk of cardiovascular diseases: results from the prospective NutriNet-Santé cohort	NME	9	No
Carcinogenicity of occupational exposure as a firefighter	ESC	9	Yes
Current and future burden of breast cancer: Global statistics for 2020 and 2040	CSU	8	Yes
Co-benefits from sustainable dietary shifts for population and environmental health: an assessment from a large European cohort study	NME	7	No
Maternally Orphaned Children and Intergenerational Concerns Associated with Breast Cancer Deaths Among Women in Sub-Saharan Africa	ENV	7	No
The European response to the WHO call to eliminate cervical cancer as a public health problem	Multiple PI	7	No
Vaccine efficacy against persistent human papillomavirus (HPV) 16/18 infection at 10 years after one, two, and three doses of quadrivalent HPV vaccine in girls in India: a multicentre, prospective, cohort study	EPR	7	Yes
2020 list of human papillomavirus assays suitable for primary cervical cancer screening	EPR	7	No

Dietary Fatty Acids, Macronutrient Substitutions, Food Sources and Incidence of Coronary Heart Disease: Findings From the EPIC-CVD Case-Cohort Study Across Nine European Countries	NME	7	No
Consumption of ultra-processed foods associated with weight gain and obesity in adults: A multi-national cohort study	NME	7	Yes
Tobacco smoking changes during the first pre-vaccination phases of the COVID-19 pandemic: A systematic review and meta-analysis	CSU	6	No
Age-specific burden of cervical cancer associated with HIV: A global analysis with a focus on sub-Saharan Africa	CSU	6	Yes
Epidemiology of anal human papillomavirus infection and high-grade squamous intraepithelial lesions in 29 900 men according to HIV status, sexuality, and age: a collaborative pooled analysis of 64 studies	EPR	5	Yes
The IARC Perspective on Cervical Cancer Screening	ESC	5	Yes

Main references and documents

- IARC MTS 2021-2025
- MTS evaluation framework and KPIs
- MTS evaluability assessment
- Director's annual reports:
  - ➔ 2023
  - ➔ 2022
  - ➔ 2021
- Biennial report
  - ➔ 2022-2023
  - ➔ 2020-2021
- Reports of the Scientific Councils
  - ➔ SC60
  - ➔ SC59
  - ➔ SC58
- Biennial report on publications:
  - ➔ 2022-2023
  - ➔ 2020-2021
- Financial reports:
  - ➔ FY2023
  - ➔ FY2022
  - ➔ FY2021