International Agency for Research on Cancer

World Health Organization

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EVALUATION REPORT ON THE IMPLEMENTATION OF THE IARC MEDIUM-TERM STRATEGY (MTS) (2016–2020)

A. Summary

1. This review of the IARC Medium-Term Strategy (2016–2020) (MTS) is the first time the Agency has reviewed overall progress in this format. The reporting period covers 2.5 years from January 2016 to June 2018, i.e. half the full period covered by the MTS.

2. The document comprises three parts: a summary describing some of the highlights; a set of quantitative MTS evaluation indicators; and a series of case studies that illustrate in a qualitative manner specific contributions towards the MTS. Much of the Agency's research output cannot be captured in quantitative indicators and thus the case studies complement other information provided to the Scientific and Governing Councils. All three parts of the document should be taken into account when reviewing progress in implementing the MTS.

3. The Scientific Council has emphasized that the five-year peer-review cycle of the scientific Groups and Sections remains the primary method for an in-depth assessment of performance and alignment with the Agency's mandate. In addition, the Scientific Council also reviews specific programmes and activities on an annual basis. The majority of IARC's work is subject to further external peer-review, either at the stage of application for funding or when research is published in peer-reviewed journals. The Director has provided over the last decade an annual written report to the Governing Council, which includes a standard set of key performance indicators (KPIs).

4. This review of the MTS is intended to provide a broader overview of the directions and progress of the research activities at IARC. The MTS evaluation indicators on which this report is structured were defined by a Joint Governing and Scientific Council Working Group, which included the IARC secretariat and representation from WHO. The evaluation indicators were adopted by the Governing Council at its 59th session (see Resolution GC/59/R6).

5. In reporting on a strategy stretching over several years, it is important to recognize the dynamic nature of research. Results from one study may lead to significant changes in approach to the underlying question being addressed. Exciting opportunities arise for new international collaborations that cannot be envisaged even months, let alone years, in advance. Plans may be modified or dropped completely because of lack of funding, because a pilot phase indicates a lack of feasibility or for a range of logistic reasons. Thus evaluating research outputs is recognized as challenging and multi-faceted. IARC is somewhat unique in being a research organization within the broad UN family and approaches taken to evaluating its activities need to reflect that fact.

6. This first overall review of the MTS has provided valuable experience in gathering and interpreting data for the evaluation indicators and case studies as set by the Governing Council in Resolution GC/59/R6. As a result it is recommended that lessons learned from this exercise be used to refine future review processes, recognizing that some proposed elements were not possible to measure or proved to be uninformative.

7. A number of highlights and main conclusions from the analyses of the MTS evaluation indicators and case studies are provided below.

8. The **high quality and demand for the Agency's research** is clearly illustrated in the evaluation indicators relating to publications and related materials (see Section 1.1 – publications in scientific journals; Section 1.2 – other types of publications):

- IARC's research is published in high-impact scientific journals – more than half (55%, see Table 4) of the articles appeared in the top 20% of journals in their subject categories.
- The publications have a high impact, as measured both through traditional (journal citation-based metrics) and novel indicators that measure citations in online sources (Altmetrics – Figures 1 and 2).
- IARC papers rank consistently amongst the highest cited research outputs tracked by Altmetrics (Figures 2 to 4).
- There is high demand for IARC's outputs, illustrated by the continued sales of the IARC/WHO Blue Books (Tables 7 and 8) and the number of visits to and downloads from IARC websites (Tables 9 and 10).

9. It is also notable that the quality of scientific output is consistent across all areas of activity, i.e. in the different areas of the MTS Project Tree (see Table 5) and that the relationship between the relative productivity of publication outputs when compared to the investment made is maintained across all areas (see Table 6). This is consistent with the outstanding external peer-review results for all research Sections over the last five-year cycle.

10. The Agency scientists have been **successful in attracting extrabudgetary funding** (see Section 1.3 – Research competitiveness; ability to attract extrabudgetary funding)

- Over the 2.5 years of the review IARC scientists have participated in collaborative funding awards to a total value of €68 million of which €25 million has been assigned to the Agency (Table 11).
- The high proportion of funding assigned to IARC collaborators (Table 12) demonstrates the Agency's role in catalysing research, bringing funding to a wide network of national institutions worldwide.
- Agency scientists invest significant time and effort to obtain extrabudgetary funds. There has been a steady increase in the number of funding applications (36% increase) and signed contracts (21% increase) in the review period compared to the previous MTS (Table 13).
- It is notable that just under 200 funding applications are made annually by Agency scientists while the number of professional grade scientists funded on the regular budget is only around 50, including junior positions.
- The success in generating funds represents a good "return on investment" for Participating States from assessed contributions. For each €1 of the regular budget invested in research, Agency scientists added €0.68 from extrabudgetary contracts (Table 14, €11.4 million spent on extrabudgetary funds for €16.8 million on regular budget).

11. As with publications, the data on funding show a consistency across the different areas of the MTS Project Tree and a strong correlation with the investment made in each area (Table 15).

12. The Agency makes a **remarkable contribution to capacity building** in its areas of expertise (see Section 2.1 – Developing human resources). A number of features of the education and training activities merit highlighting:

- Around half of Early Career and Visiting Scientists (53%, excluding local French trainees) and IARC Postdoctoral Fellows (58%) originate from Participating States (Figures 5 and 6).
- A large proportion of IARC postdoctoral positions are awarded to scientists from low- and middle-income countries (LMICs), particularly for the Fellowship Programme (73%) (Figures 5 and 6 and Table 16).
- The number of courses, attendees and countries in which courses are held have all increased two to three-fold compared to the previous MTS reporting period (Table 17), due in part to a strategic shift towards e-learning events.
- There is a clear focus on courses to train scientists in LMICs, with 80% of courses and 84% of participants originating from these regions (Figure 7).
- The Agency has begun to record and make available online an increasing number of seminars and webinars (see Tables 18 to 20) with the goal of using the limited resources available to reach the widest possible audience.

13. The Agency has an outstanding record in **catalysing international collaborations** as evidenced by a number of the evaluation indicators (see Section 2.3 – Developing collaborative networks):

- In the short period under consideration, IARC has published scientific articles with collaborators from 141 countries out of the total of 195 worldwide; this demonstrates a quite remarkable reach for an Agency of this size.
- The Agency has extensive collaborations with scientists in Participating States; of the top 20 countries that IARC scientists publish most frequently with, 18 are Participating States; a similar pattern is seen for funding awards (Figures 8 to 11).
- In a comparison with “benchmark organizations” (Table 21) IARC has far higher levels of co-authorship with international collaborators.
- The Agency has long-term collaborations (as judged by joint publications, grants and consortia) with a large number of LMICs (Figures 8 to 11).
- The collaborations on grants with LMICs are particularly important in terms of impact, providing resources for the development of local research capacity.
- The figures for the total number of countries with whom IARC collaborates in the context of international research consortia confirm those obtained in the bibliometric analyses (129/195 and 141/195 respectively).
- IARC coordinates 20 consortia (Table 23) which involve 978 partner institutions and participates in a further 16 collaborative consortia comprising 542 partner organizations. These consortia cover the full spectrum of IARC’s MTS areas on cancer occurrence, causes, prevention, capacity building and shaping the international cancer research agenda.

14. The report presents **35 case studies that are selected to represent all areas of the Project Tree** within the MTS. This is the first time IARC has provided such examples in a standardized way, structured to cover and illustrate the full range of the Agency's work. It should be noted that these are a small selection of the projects that could have been used for purposes of a case study. A number of these are mentioned below but the full set should be consulted in the review process. Those selected for inclusion highlight a number of key features about the research of the Agency:

- **Impact on policy – IARC papers and other publications:** The scientific evidence-base produced by IARC is frequently used by WHO and national and international organizations to develop guidelines, recommendations and policies. One example is the work in India and Costa Rica on less than three doses of HPV vaccine (case study #1), which has been used by WHO in recommending two doses and referenced by the National Cancer Institute, USA in deciding to fund a trial of one dose of HPV vaccine. Another example is the IARC Monograph evaluation of artificial tanning devices (case study #5) which has been a basis for legislation in several countries leading either to bans or placing age restrictions on use.
- **International collaborations – grants:** A feature of the Agency is its ability to bring together networks of researchers to make joint applications for major grant funding. In the Mutographs project (case study #9) IARC brought together research centres across five continents to collect 5000 tumours of five different types to investigate the international variation in cancer genomes. This project attracted a £20 million grant and promises to be informative for studies of both etiology and treatment. It is difficult to imagine any other organization able to bring together so many diverse collaborators. In Latin America IARC is coordinating a multi-centre study on cervical cancer screening methods linked to HPV DNA testing (ESTAMPA, case study #10). Here there is no single major funder involved. Rather the study illustrates a different model of how the Agency works with the national partners successful in leveraging resources for this ground-breaking study because they are part of an IARC-led collaboration applying a standardized protocol.
- **International collaborations – IARC-led partnerships and consortia:** The Agency's position as an international research organization with reputation for excellence enables it to lead many major consortia, bringing leading experts together to address a cancer control research priority. A prime example is AGRICOH (case study #14) whereby a number of national studies on cancer in agricultural workers have been combined to permit a more detailed analysis of pesticide exposure and cancer risk. Research in LMICs provides much needed evidence for cancer control while simultaneously building capacity among a new generation of cancer researchers. An excellent example is ESCCAPE (case study #16) where the Agency has established collaborations across east and southern Africa to understand the extremely high oesophageal cancer rates. This work is revealing completely new insights into risk factors that are amenable to public health interventions, while also building research capacity in this model "partnership of equals".
- **International collaborations – consortia in which IARC is a partner:** There are collaborations where IARC brings a unique expertise or strength to a partnership but is not the lead organization. A good example is the International Childhood Cancer Cohort Consortium (I4C) (case study #19). This group is focused on early life exposures and childhood cancer. IARC's expertise and leadership in looking at genetic alterations consequent to environmental exposures early in life added a fresh dimension to the consortium and is now providing mechanistic data to investigate epidemiological studies of exposure/disease associations. The longstanding commitment of IARC to the

International Association of Cancer Registries (case study #20), through support of the Secretariat, has been instrumental in building the multi-partner Global Initiative on Cancer Registry Development (GICR). The IACR has over 500 members worldwide.

- **International collaborations – research platforms:** The Agency may initiate a specific study that transforms into a platform for future research or it may deliberately establish such platforms in perceived areas of need. An example of the latter is the Biobank and Cohort building Network (BCNet) (case study #22) that provides training, support and advice on adapting state-of-the-art biobanking practices to LMICs, with a particular focus on Africa. Biobanking is a key to developing cancer research in LMICs and yet the requisite knowledge transfer is often lacking; BCNet is responding to that need. The HPV-AHEAD (case study #21) extended IARC's collaboration on HPV and human cancers in India. As a part of that collaboration IARC and the German Cancer Center (DKFZ) transferred the laboratory technology for HPV analysis to the partner laboratory in India; all analyses are now performed locally, with quality control provided by the Agency and our German partners.
- **Provision of expertise for national policy development:** IARC's close research cooperation with national colleagues naturally leads to requests for expert advice, guidance, support and training in translating scientific knowledge into practice. For example IARC partners with the International Atomic Energy Agency (IAEA) and WHO on the IAEA-led imPact missions to advise countries on cancer control planning (case study #24). IARC provides its expertise on cancer registration and screening. IARC also works with countries to implement cancer control programmes, building a research component into a pilot phase or early stage roll-out of programmes in order to enable further refinement of the approach taken. Good examples include colorectal cancer screening (case study #25) or HPV vaccination in low-income countries (case study #27).
- **Provision of expertise for international policy development:** The Agency conducts a number of activities that support major strategic policy-related areas. A leading example is the GICR. In this collaboration (case study #28) the Agency has brought together a wide range of partners to develop a coordinated strategic approach to developing registries in LMICs. IARC Regional Hubs and Collaborating Centres have been established worldwide providing a devolved structure with technical expertise and support from IARC. This approach is transforming cancer registration globally. IARC established the consortia entitled "Cancer Prevention Europe" (case study #30) among a number of leading centres in Europe in order to shape the European cancer research agenda and to promote the case for prevention. Finally IARC produces the WHO Classification of Tumours series (case study #31). These volumes underpin clinical oncology as well as serving cancer registration and research. In producing the books IARC has assembled a strong international editorial team of leading pathologists and engages around 1800 authors across the full series of volumes.
- **Development of new methodologies and open access tools:** One way in which the Agency contributes to the public goods of the cancer community is by developing open source software and other tools for researchers. The development of cancer registries is supported by the CanReg5 open source software (case study #32). The Agency provides training and technical support to users worldwide. In a completely different domain, that of bioinformatics (case study #33), IARC has also been developing open access tools to provide benefit to users outside the Agency where the capacity is lacking; this development has emerged from IARC's recent investment in computational biology.

- **Training for cancer research:** The IARC postdoctoral programme (case study #34) has been a key part of the IARC capacity building efforts since the inception of the organization. Many fellows remain in cancer research, return to their home countries and continue to collaborate with IARC subsequent to their training period.
- **Supporting the efficient conduct and coordination of research:** As the Agency prepares for its new headquarters in Lyon (Nouveau Centre, case study #35) the principle being followed is one of opening doors to the local, regional, national and international cancer community. The auditorium and other meeting rooms will be available to local researchers as well as being a meeting point for scientists internationally. The IARC Biobank will house unique collections of samples from collaborators around the world, ensuring a secure place for storage, sample preparation and distribution within a robust ethical and legal framework.

15. This report provides a basis for the Scientific and Governing Councils to review IARC's progress in implementation of the current MTS (2016–2020). The different ways of presenting the work, through evaluation indicators and case studies, provide valuable insights but still cannot do justice to the full breadth of the research, achievements and impact over the past 2.5 years.

16. The review should also be interpreted in the context of the annual regular budget of the Agency, which stands at €22 million. It would be valuable if the Agency and its governing bodies, in making evaluations in the future, could find a valid and reliable way to assess the achievements against investment in comparison to bench-marked national and international research organizations.

B. Quantitative MTS evaluation indicators

IARC Reporting category

1. ADVANCING KNOWLEDGE FOR CANCER PREVENTION THROUGH RESEARCH

1.1. PUBLICATIONS IN SCIENTIFIC JOURNALS

1.1.1 Bibliometric analyses

A total of 914 articles published by IARC authors from Jan. 2016 to June 2018[1] were included in the analyses. All IARC articles published in this period were reviewed individually and classified into the four main scientific categories of the IARC MTS 2016–2020 Project Tree (Level 2 objectives – see Table 1). Each article was classified into a single category depending on its main topic. Articles that resulted from methodological collaborations or sharing of samples and data on topics not directly related to the four Project Tree categories were not included in the analyses.

Table 1: Classification of IARC articles published from Jan. 2016 to June 2018 according to the Level 2 objectives of the IARC Project Tree

IARC Project Tree 2016-2020 Level 2 objectives		Number of articles	%
Describe the occurrence of cancer	PT-1	133	14.6%
Understand the causes of cancer	PT-2	566	61.9%
Evaluate and implement cancer prevention and control strategies	PT-3	102	11.2%
Increase the capacity for cancer research	PT-4	50	5.5%
Not classified		63	6.9%

The majority of papers were classified in area PT-2, reflecting the overall distribution of projects in the Project Tree. Area PT-2 represents the largest field of activity of the Agency, both in terms of regular budget and number of staff (see below). Understanding the causes of cancer is a prerequisite for proceeding to studies of preventive interventions which are the focus of PT-3. The mechanistic research conducted in the Agency's laboratories is placed within PT-2 although its relevance to PT-3 should be noted. In addition PT-2 includes most of the large research consortia the Agency leads or participates in, which result in a substantial number of collaborative publications.

[1] Limited to papers indexed in Web of Science by 30 June 2018

1.1.1.1 *Total number of papers (sub-categorized by peer reviewed articles; letters to the Editor or comments; invited reviews; editorials/news and other)*

Table 2 shows the breakdown of IARC scientific papers published during the reporting period by year and by type of article. A slight increase in the average total number of articles and in the proportion of peer-reviewed papers was observed in relation to the previous MTS. The large majority of publications (>80%) are therefore original articles containing novel research data.

Table 2: IARC papers published from Jan. 2016 to June 2018

Year	Total	Peer-reviewed articles	(%)	Letters to Editor or comments	Invited reviews	Editorials, news, other
2016	341	290	(85%)	9	28	14
2017	352	291	(83%)	12	25	24
Jan-June 2018	166	135	(81%)	6	17	8
Average[1]	343.6	286.4	(83.4%)	10.8	28	18.4
Average previous MTS (2010–2015)	332.0	268.0	(80.7%)	11.3	31.8	20.8

[1] Averages for the current MTS in this and in subsequent tables were calculated on the basis of the projection for the full year of 2018.

Table 3 shows the breakdown of IARC scientific papers published during the reporting period by Project Tree Level 2 objectives and by type of article. There are no major differences in pattern of publication types across the areas.

Table 3: IARC papers published from Jan. 2016 to June 2018 by Project Tree Level 2 objectives

MTS Project Tree Area	Total	Peer-reviewed articles	(%)	Letters to Editor or comments	Invited reviews	Editorials, news	Other
PT-1	133	100	(75%)	7	10	10	6
PT-2	566	470	(83%)	17	44	15	20
PT-3	102	70	(69%)	1	12	11	8
PT-4	50	40	(80%)	0	6	4	1

1.1.1.2 *Number/proportion of IARC papers published in top 20% of journals in their subject category*

Overall, 55% of articles published by IARC scientists in the reporting period appeared in the top 20% of journals in their subject categories, according to the classification in the Thomson Reuters databases (Web of Science and Journal Citation Reports – see Table 4). This is broadly in line with the results for the previous MTS.

Table 4: IARC papers published in top 20% of journals in their subject category from Jan. 2016 to June 2018.

Year	Number of IARC papers in all journals in all SC[1]	Number of IARC papers in top 20% journals in all SC	% of IARC papers in top 20% journals in all SC
2016	511	275	54%
2017	482	277	57%
Jan-Jun 2018	223	131	59%
Average	495	271	55%
Average previous MTS (2010-2015)	N.A.	N.A.	60.5%

[1] A given journal can appear in more than one subject category

N.A. – Data not available

Table 5: IARC papers published in top 20% of journals in their subject category from Jan. 2016 to June 2018 by Project Tree Level 2 objectives (only the top 5 subject categories for IARC papers in each Project Tree main area are shown)

All areas

JOURNAL SUBJECT CATEGORY	Total number of journals in SC	Number of IARC papers in all journals in the SC	Number of IARC papers in top 20% journals in SC	% of IARC papers in top 20% journals in SC
ONCOLOGY	222	336	158	47%
PUBLIC ENVIRONMENTAL OCCUPATIONAL HEALTH	179	193	97	50%
NUTRITION DIETETICS	79	76	29	38%
MULTIDISCIPLINARY SCIENCES	64	61	34	55%
MEDICINE GENERAL INTERNAL	154	55	40	73%

PT-1 – Describe the occurrence of cancer

JOURNAL SUBJECT CATEGORY	Total number of journals in SC	Number of IARC papers in all journals in the SC	Number of IARC papers in top 20% journals in SC	% of IARC papers in top 20% journals in SC
ONCOLOGY	222	82	33	40%
PUBLIC ENVIRONMENTAL OCCUPATIONAL HEALTH	179	53	13	25%
MEDICINE GENERAL INTERNAL	154	11	6	55%
GASTROENTEROLOGY HEPATOLOGY	80	7	7	100%
UROLOGY NEPHROLOGY	76	4	3	75%

PT-2 – Understand the causes of cancer

JOURNAL SUBJECT CATEGORY	Total number of journals in SC	Number of IARC papers in all journals in SC	Number of IARC papers in top 20% journals in SC	% of IARC papers in top 20% journals in SC
ONCOLOGY	222	211	101	48%
PUBLIC ENVIRONMENTAL OCCUPATIONAL HEALTH	179	116	75	65%
MULTIDISCIPLINARY SCIENCES	64	52	27	52%
NUTRITION DIETETICS	79	45	12	27%
MEDICINE GENERAL INTERNAL	154	31	24	77%

PT-3 – Evaluate and implement cancer prevention and control strategies

JOURNAL SUBJECT CATEGORY	Total number of journals in SC	Number of IARC papers in all journals in SC	Number of IARC papers in top 20% journals in SC	% of IARC papers in top 20% journals in SC
ONCOLOGY	222	37	22	59%
MEDICINE GENERAL INTERNAL	154	13	8	62%
OBSTETRICS GYNAECOLOGY	81	12	1	8%
PUBLIC ENVIRONMENTAL OCCUPATIONAL HEALTH	179	10	4	40%
IMMUNOLOGY	155	9	5	56%

PT-4 – Increase the capacity for cancer research

JOURNAL SUBJECT CATEGORY	Total number of journals in SC	Number of IARC papers in all journals in SC	Number of IARC papers in top 20% journals in SC	% of IARC papers in top 20% journals in SC
NUTRITION DIETETICS	79	16	6	38%
PUBLIC ENVIRONMENTAL OCCUPATIONAL HEALTH	179	8	3	38%
ONCOLOGY	222	5	2	40%
GENETICS HEREDITY	171	4	1	25%
FOOD SCIENCE TECHNOLOGY	133	4	3	75%

Overall the Agency publications have the highest percentage in the top 20% of journals in the categories of Medicine General Internal, Multidisciplinary Sciences and in Public, Environmental and Occupational Health with slightly lower percentages for Oncology and Nutrition Dietetics (Table 5). The additional comparison of the results for the different Project Tree Level 2 objectives in Table 5 is difficult to interpret, as the stratification by Project Tree area selects for publications on different journal subject categories and the small numbers result in wide variation, however the two categories that rank amongst the top 5 across all the Project Tree areas, Oncology and Public Environmental Occupational Health present broadly similar results.

1.1.1.3 *Number of papers published expressed by the number of IARC Regular Budget funded scientists*

There is a strong correlation between the percent of publications in the different Project Tree areas and the percent of Regular Budget scientific staff assigned to those areas (Table 6). This indicates consistent levels of productivity, in terms of publication outputs, across the different areas of the Agency. The slightly lower rates of publications observed for area PT-4 "Increase the capacity for cancer research" may reflect the fact that many of the activities in this area result in other types of outputs than the traditional scientific articles presented in this section of the report.

Table 6: Average distribution of IARC Regular Budget funded staff in years 2016 to 2018 according to the main areas of the IARC Project Tree, compared to the distribution of articles published Jan. 2106 to June 2018

Project Tree area	**GS staff**	**(%)**	**P staff**	**(%)**	**% all scientific staff**	**% articles published** (from Table 1)
PT-1[1]	9.7	(18.1%)	6.2	(11.7%)	14.9%	14.6%
PT-2[1]	30.3	(56.8%)	34.5	(65.1%)	60.9%	61.9%
PT-3[1]	2.0	(3.8%)	8.3	(15.7%)	9.7%	11.2%
PT-4[1]	11.4	(21.3%)	4.0	(7.5%)	14.4%	5.5%

[1] Distribution of IARC Groups by Project Tree areas for the calculation of staff numbers:
PT-1 - CSU, *MPA*, *WCT*; PT-2 - ICB, ICE, ENV, BMA, NEP, GCS, GEP, EGE, MMB, IMO;
PT-3 - GHI, PRI, SCR, *IHB*; PT-4 - ETR, LSB, *BST*, *DEX*, *NMB.*
Figures are approximate as they do not reflect the fact that Groups have activities across several Project Tree areas; Groups that were dissolved or created during the reporting period are shown in italics.

1.1.2 Indicators from non-traditional sources (ALTMETRIC)

ALTMETRIC.COM is a data science company that tracks a range of online sources to capture and collate mentions to published research. *Altmetrics* are quantitative and qualitative data that are complementary to traditional citation-based metrics (e.g. impact factor or number of citations of specific papers in other scholarly articles). They can include citations in online reviews, on Wikipedia, in public policy documents, discussions on research blogs, mainstream media coverage, bookmarks on reference managers, and mentions on social networks such as Twitter.

The analyses shown below are limited to a set of 934 journal articles[2] published by IARC from Jan. 2016 to June 2018. Figure 1 shows a comparison of the distribution of ALTMETRIC attention scores of IARC articles and of the attention scores of all the research outputs tracked by ALTMETRIC in the same period. In the top category 9% of all IARC articles received an attention score >100 compared to just 2.2% of all research outputs combined. Although this is a somewhat crude metric it demonstrates that IARC articles generate substantially more attention, i.e. are cited more frequently, in the online sources tracked by ALTMETRIC than other similar research outputs.

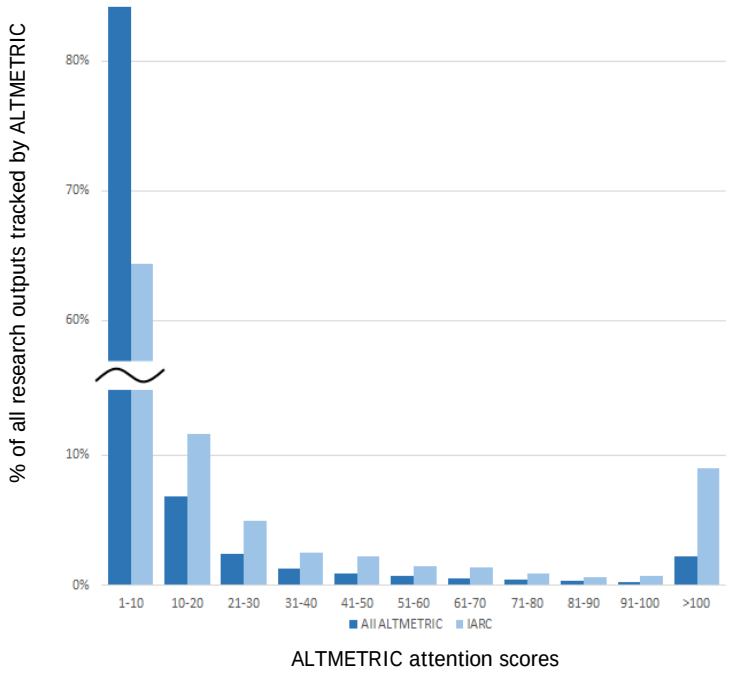


Figure 1: ALTMETRIC attention scores (weighted count of all of the mentions tracked by ALTMETRIC for an individual research output) for IARC articles published in Jan. 2016 to June 2018 compared to all items in ALTMETRIC published in the same period.

Figure 2 provides a comparison of the average ALTMETRIC attention scores of IARC papers in a given journal versus the average attention scores for all items published in that journal, stratified for each ALTMETRIC category. The analysis shows, for example, that IARC papers in the *International Journal of Cancer* were on average 10 times more likely to be cited in a policy source than the other items in that journal over the same period, and conversely approximately 6 times less likely to be mentioned in news items tracked by ALTMETRIC. The results for the *British Journal*

[2] This number of articles is different from the one in the section above as ALTMETRIC includes papers published during the reporting period but not yet indexed in Web of Science.

of Cancer, *The Lancet* and *The Lancet Oncology* are noteworthy, demonstrating the very high levels of attention generated by IARC articles published in these journals across the range of online sources tracked by ALTMETRIC.

Relative citations in policy sources are notably elevated not only for IARC papers in the International Journal of Cancer but also in the International Journal of Epidemiology, The Lancet and Lancet Oncology (Figure 2).

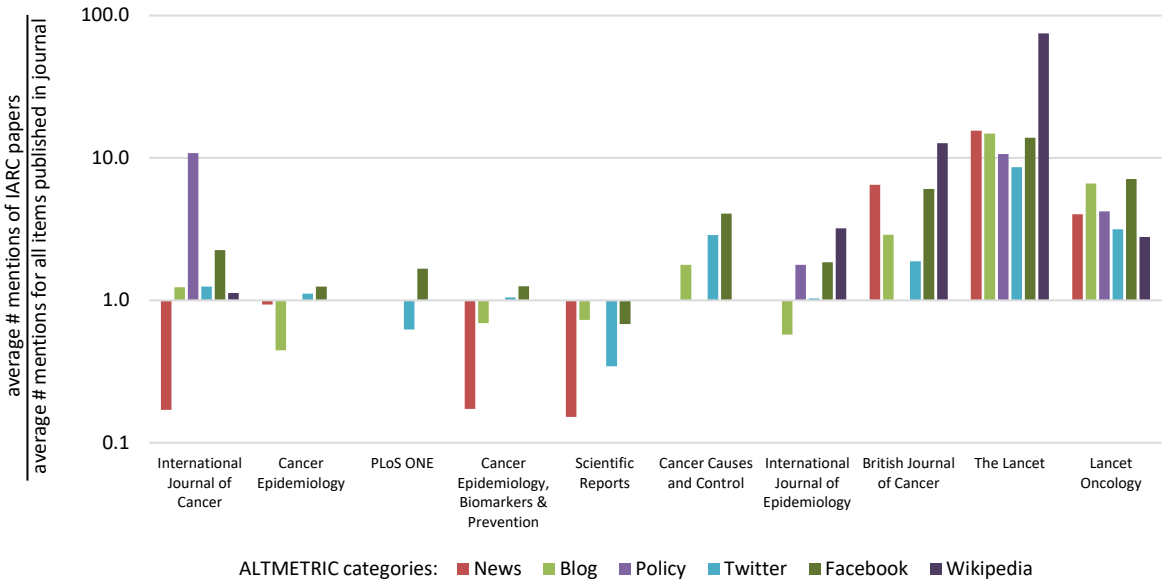
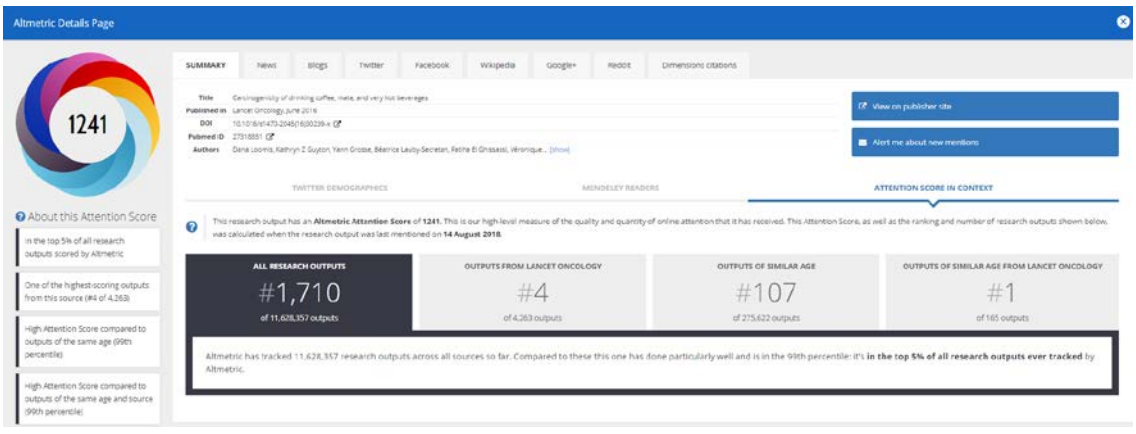


Figure 2: Rates of the average number of mentions of IARC papers published in a given journal (for the top 10 journals where IARC papers were published in Jan. 2016 to June 2018) vs the average number of mentions for all items published in that journal in the same period, stratified by ALTMETRIC category (note: the y axis is a log scale).

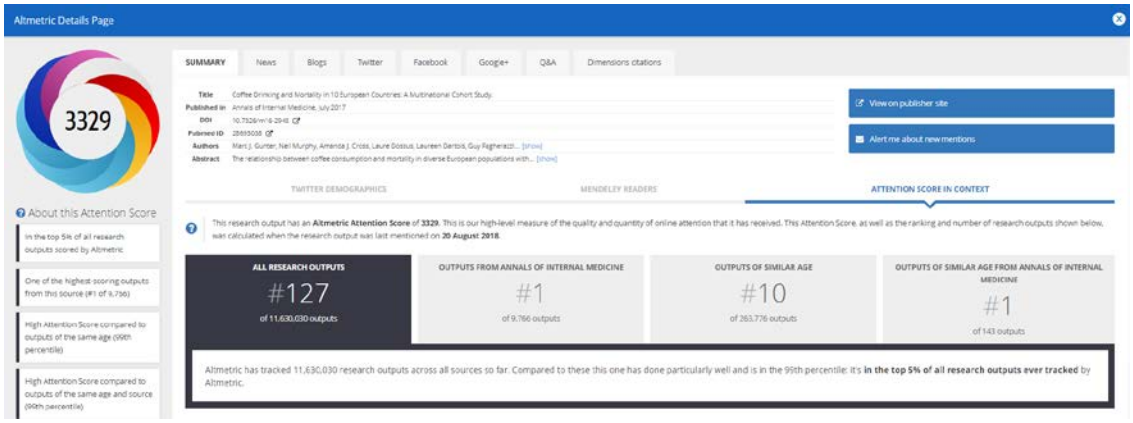
A more direct illustration of the impact of IARC outputs is the ranking of IARC articles by ALTMETRIC attention score (Figures 3 and 4). Remarkably, the three IARC articles with the highest attention scores in 2016, 2017 and first half of 2018 all rank #1 in the respective journals when compared to all articles published in that journal of a similar age (furthest right column in screen shots below).

The same articles rank #1 to #4 when compared to all articles published in those journals since the start of ALTMETRIC (second column, Figure 3). Of particular note is the paper on *"Coffee Drinking and Mortality in 10 European Countries: A Multinational Cohort Study"* published in *Annals of Internal Medicine* in 2017 which ranks #127 of all 11.6 million research outputs ever tracked by ALTMETRIC (left hand column, Figure 3).

2016



2017



2018

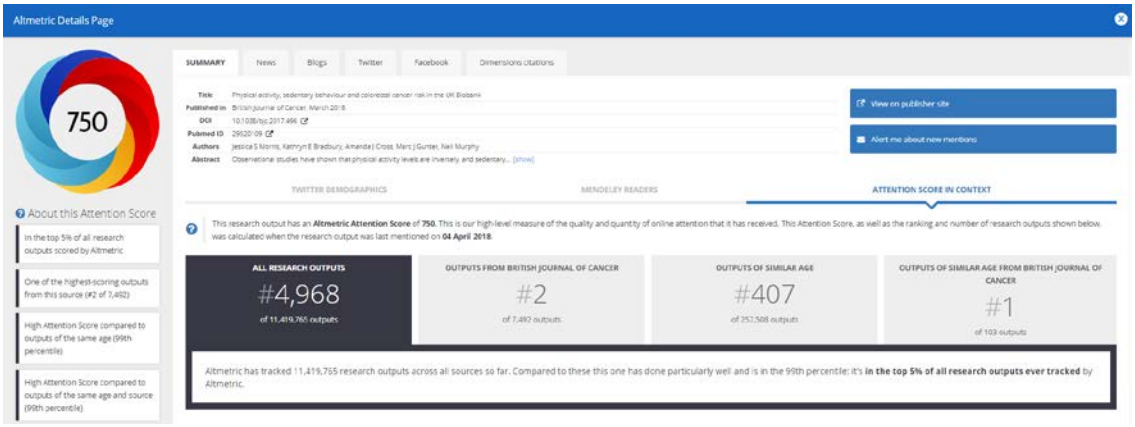


Figure 3: "ALTMETRIC Score in Context" for the top IARC-led articles published in each of the years covered in this evaluation.

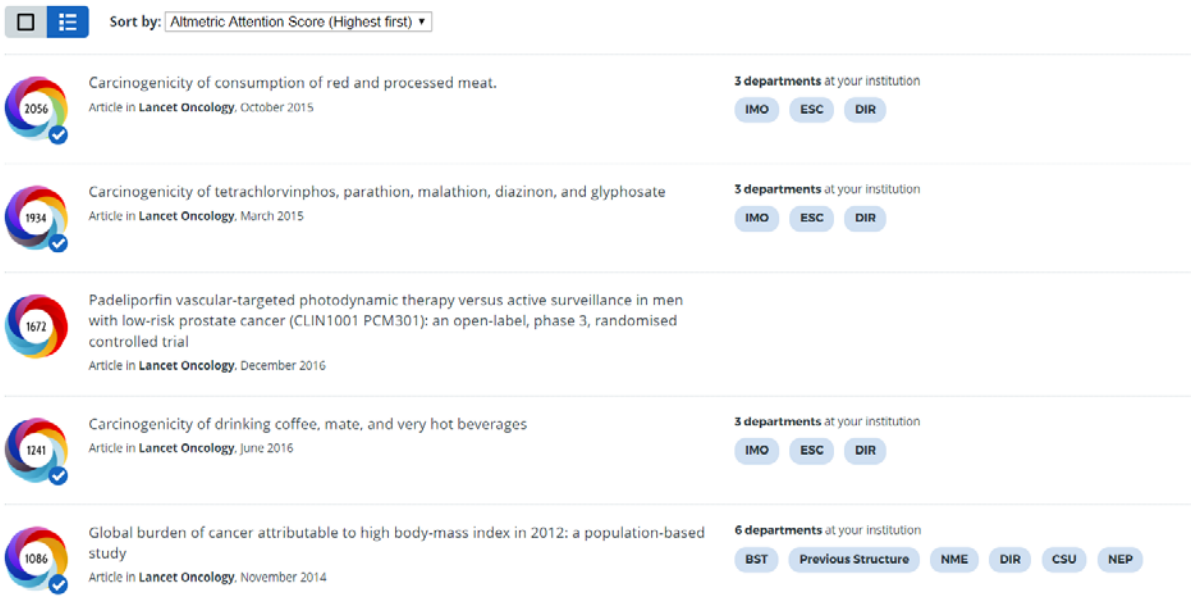


Figure 4: Five top ranking articles published in *The Lancet Oncology* according to "ALTMETRIC Attention Scores".

Of the five top ranking articles of all time, as measured by "ALTMETRIC Attention Scores", in the Lancet Oncology, three are from IARC (Figure 4).

1.1.2.1 *Number of policy documents which have cited IARC's papers*

It was expected that Altmetrics would provide an additional layer of information on the impact of IARC's research, including for outputs other than scientific papers (e.g. IARC websites, IARC serial publications, etc.) and in particular that it would provide data on the citations of IARC's research in policy documents.

After loading IARC's data on ALTMETRIC and reviewing its functionalities it was apparent that IARC books were not tracked reliably and that the coverage and tracking of policy sources were not sufficiently developed to enable a comprehensive analysis. For this reason the policy impact of IARC scientific papers and other types of publication is currently better illustrated through representative case studies.

1.2 OTHER TYPES OF PUBLICATIONS

1.2.1 Access to IARC publications and resources

1.2.1.1 *Volume of sales of printed publications*

1.2.1.2 *Volume of sales of e-publications from IARC e-bookshop*

1.2.1.3 *Total revenue from sales of IARC publications (proportion of revenue from sales of Blue Books)*

A total of 70 797 print copies of IARC publications were sold in the period Jan. 2016 to June 2018 (see Table 7), with nearly all of the sales (99%) due to the WHO Classification of Tumours Series ("Blue Books"). These figures are around double those for the previous MTS period. Together with those on the revenue from sales, which have also doubled (see Table 8), they reflect the strong development of the IARC publications programme, and in particular the growing success of the WHO/IARC Classification of Tumours.

The e-bookshop has only been operational for two years of the reporting period but the number of free downloads is growing. The number of purchases through this route is small but expected to develop as new volumes are added.

Table 7: Publications – Volume of sales of print and e-publications

Year	Total sales	Sales of 'Blue Books'	Freely downloaded e-books	Purchased e-books
2016	25 295	24 677 (98%)	8 651	167[1]
2017	33 786	33 544 (99%)	11 422	191
Jan-June 2018	11 716	11 659 (99%)	5 776	42
Average	27 504	27 180 (99%)	12 946	200[1]
Average previous MTS (2010–2015)	15 281	14 359 (94%)	N.A.	N.A.

[1] From the start of the e-bookshop on 1 June 2016
[2] Average over two years from June 2016 to June 2018

Table 8: Publications – Revenue from sales (Swiss Francs)

Year	Revenue from sales of all publications	Revenue and percent from 'Blue Books'	Revenue from sales paid to IARC[1]	Other revenue (ePub and royalties)
2016	1 450 727	1 436 443 (99.0%)	1 450 172	15 795
2017	1 756 548	1 752 327 (99.8%)	1 751 567	12 201
Jan-June 2018	709 095	708 027 (99.8%)	N.A.	N.A.
Average	1 541 822	1 534 941 (99.6%)	1 600 870	13 998
Average previous MTS (2010–2015)	783 925	758 077	761 148	N.A.

[1] After charges were deducted from overall figure
N.A. – Figures not yet available; averages based on figures for 2016 and 2017 only

1.2.1.4 *Number of downloads of online/pdf publications from IARC websites*[3]

1.2.1.5 *Number of visits to IARC online databases*

Over the review period there were 16 IARC publications which received 100 000 or more downloads from the website (Table 9). Of the top 20 downloads, twelve were Monographs, four "Blue books" and one a Handbook of Cancer Prevention reflecting the importance of these flagship programmes to the wider cancer community. The six-part volume 100 of the IARC Monographs summarizes data on carcinogenic agents classified Group 1 and four of the six appear on the list.

It is also notable that key publications from two areas of "core" IARC expertise for training were also among the top 20. The volume on "Cancer Epidemiology: Principle and Methods" although published in 1999 received the highest number of downloads with almost 437 000 over the review period. The IARC Scientific Publication No. 95 on cancer registration "Cancer Registration: Principles and Methods" published in 1995 is still a standard reference for the field. Both these volumes are scheduled for new editions during the current MTS publication.

Table 9: Top 20 downloaded publications from the IARC and Monographs websites for the period Jan. 2016 to June 2018

Item	Number of downloads
Cancer Epidemiology: Principles and Methods	436 948
Monograph Volume 100E: Personal Habits and Indoor Combustions	425 459
Monograph Volume 100F: Chemical Agents and Related Occupations	397 135
Monograph Supplement 7: Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs Volumes 1 to 42	325 670
Monograph Volume 100C: Arsenic, Metals, Fibres and Dusts	255 966
IARC Handbook of Cancer Prevention Volume 8: Fruit and Vegetables	218 121
"Blue Book" Pathology and Genetics of Tumours of the Digestive System – Third Edition	176 039
Monograph Volume 100A: Pharmaceuticals	175 359
Monograph Volume 99: Some Aromatic Amines, Organic Dyes, and Related Exposures	166 479
Monograph Volume 82: Some Traditional Herbal Medicines, Some Mycotoxins, Naphthalene and Styrene	160 336
World Cancer Report 2003	148 494
"Blue Book" Pathology and Genetics of Tumours of Soft Tissue and Bone – Third Edition	140 406

[3] Data on access to IARC resources hosted in external websites could not be included

Item	Number of downloads
"Blue Book" Pathology and Genetics of Head and Neck Tumours – Third Edition	135 588
IARC Scientific Publication No. 95: Cancer Registration: Principles and Methods	124 165
"Blue Book" Pathology and Genetics of Tumours of the Lung, Pleura, Thymus and Heart – Third Edition	118 834
Monograph Volume 108: Drugs and Herbal Products	101 221
Monograph Volume 109: Outdoor Air Pollution	98 657
Monograph Volume 93: Carbon Black, Titanium Dioxide, and Talc	93 949
Monograph Volume 112: Some Organophosphate Insecticides and Herbicides	93 608
Monograph Volume 83: Tobacco Smoke and Involuntary Smoking	91 313

In relation to the visits to IARC online databases, GLOBOCAN with 1.2 million visits continues to be by far the most popular IARC database, followed by the IARC TP53 Database and the new Global Cancer Observatory (GCO) launched for the Governing Council session in May 2016 tops the list (Table 10), both with close to 250,000 visits during the review period. Indeed with the exception of the TP53 database all the remaining databases are part of the GCO. This demonstrates the role of IARC in being the definitive resource on global cancer statistics for WHO.

Table 10: Number of visits to IARC online databases for the period Jan. 2016 to June 2018

Databases[1]	Number of visits	Period
GLOBOCAN 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012	1 220 606	01/01/2016-30/06/2018
The IARC TP53 Database	247 698	01/01/2016-30/06/2018
Global Cancer Observatory	246 305	12/05/2016-30/06/2018
Cancer Today	149 151	12/05/2016-30/06/2018
Cancer and Obesity	140 406	01/01/2016-30/06/2018
CI5: Cancer Incidence in Five Continents	100 868	01/01/2016-30/06/2018
ECO: European Cancer Observatory	154 938	01/01/2016-30/06/2018
NORDCAN: Cancer Incidence, Mortality, Prevalence and Survival in the Nordic Countries	85 782	01/01/2016-30/06/2018
WHO Cancer Mortality Database	64 320	01/01/2016-30/06/2018

[1] It was not possible to include data on access to the Exposome Explorer database as this is hosted externally and the data were not available

1.3 RESEARCH COMPETITIVENESS; ABILITY TO ATTRACT EXTRABUDGETARY FUNDING

1.3.1 Analyses of grant applications

1.3.1.1 *Total value and percentage of signed contracts (with breakdown between direct funding and grants)*

Over the 2.5 years of the mid-term review IARC scientists have participated in collaborative funding awards to a total value of €68 million of which €25 million in extrabudgetary funds has been assigned to the Agency (Table 11).

The value of signed contracts reflects the fact that area PT-2 (Understand the causes of cancer) is the largest among the research activities of the Agency and thus is responsible for the most direct funding agreements and grants. This is followed by area PT-3 (Evaluate and implement cancer prevention and control strategies) (see Tables 11 and 12).

Table 11: Value of extrabudgetary funding secured from Jan. 2016 to June 2018 in direct funding agreements and grants, for each of the main areas of the IARC Project Tree (in million €)

Project Tree area	Total value of signed contracts[1]			Value attributed to IARC		
	Direct funding	Grant funding	Total	Direct funding	Grant funding	Total
PT-1	1.77	0.13	1.89	1.77	0.13	1.89
PT-2	2.22	48.29	50.50	1.62	14.22	15.84
PT-3	2.78	7.13	9.91	2.78	2.37	5.15
PT-4	0.87	4.91	5.77	0.87	0.99	1.86
PT-5[2]	0.18	0.02	0.20	0.18	0.02	0.20
Grand total	**7.81**	**60.47**	**68.27**	**7.22**	**17.72**	**24.93**

[1] The figures show total budgets of all grants signed irrespective of whether IARC is coordinating the studies or not.

[2] PT-5 – "Provide strategic leadership and enhance the impact of the Agency's contribution to global cancer research".

1.3.1.2 *Value of signed contracts attributed to IARC*

The high proportion of the total value of signed contracts assigned to IARC collaborators (see Table 12), particularly in areas PT-2 and PT-4 (Increase the capacity for cancer research), demonstrates the important role of the Agency in making research funding available to a wide network of institutions and organizations at national level.

Conversely, the very high proportion of direct funding in areas PT-1 and PT-5, which is typically attributed to support core IARC activities, explains the absence of funding to outside collaborators in these areas.

Table 12: Value of extrabudgetary funding secured from Jan. 2016 to June 2018, for each of the main areas of the IARC Project Tree, showing the proportion of funds attributed to IARC (in million €)

Project Tree area	Total value of signed contracts[1]	(% Grand Total)	Value attributed to IARC	(% attributed to IARC)
PT-1	1.89	2.77%	1.89	100%
PT-2	50.50	73.97%	15.84	31.37%
PT-3	9.91	14.52%	5.15	51.97%
PT-4	5.77	8.46%	1.86	32.24%
PT-5[2]	0.20	0.29%	0.20	100%
Grand Total	**68.27**	**-**	**24.93**	**36.52%**

There has been a steady progression in the number of applications (36% increase) and signed contracts (21% increase) in the review period compared to previous MTS (Table 13). This reflects the scientist's commitment to secure extrabudgetary funds in order to successfully implement the MTS.

It is notable that just under 200 funding applications are made annually by Agency scientists while the number of regular budget funded scientist positions is only approximately 50.

The figures for the first half of 2018 appear to show a slight drop in the number and value of signed contracts but this is likely to be an artefact linked to the calendar of grant reviews, as usually more contracts are signed in the second half of the year.

Table 13: Number of applications and value of extrabudgetary funding secured from Jan. 2016 to June 2018 (value of extrabudgetary funding in million €)

Year	Number of applications	Number of signed contracts	Total value of signed contracts[1]	Value attributed to IARC
2016	183	65	28.3	10.2
2017	193	65	38.9	11.8
Jan-June 2018	103	25	4.8	3.4
Average	191.6	62.0	28.8	10.2
Average 2010–2015	141.0	51.0	31.4	9.0

[1] The figures show total budgets of all grants signed irrespective of whether IARC is coordinating the studies or not.

1.3.1.3 *Value of Voluntary Contributions as a proportion of regular budget for scientific programme*

The figures in Table 14 show remarkably stable rates (just over 1/3) of voluntary contribution expenditure in relation to overall expenditure, representing around 35% of total expenditure at the Agency and 40% if expressed as a proportion of the regular budget assigned to the scientific activities.

The data indicate a good "return on investment" for Participating States from their assessed contributions. Specifically, for each €1 of the regular budget invested in research, Agency scientists added an additional €0.68 (Table 14, €11.4 million spent on extrabudgetary funds for €16.8 million on regular budget).

It should be noted that IARC only seeks extrabudgetary funds for activities that have been approved by the Governing Council and that fall within the defined MTS. This ensures that the agreed strategy is not deflected through a search for donor funding per se.

Table 14: Expenditure against voluntary contributions (VC), regular budget (RB) and percentage comparison (VC and RB values in million €)

Year	Voluntary contribution expenditure (VC)	Regular budget (RB)	VC / RB+VC	RB for scientific programme	VC / RB(SciProg)+VC
2016	11.4	21.4	34.8%	16.8	40.4%
2017	11.4	22.1	34.0%	16.3	41.1%
Jan-June 2018	5.7	11.0	34.2%	8.8	39.4%
Average	11.4	21.8	34.3%	16.8	40.3%
Average 2010–2015	9.7	19.2	33.6%	14.4	40.2%

1.3.1.4 *Total value of signed contracts expressed by the number of IARC regular budget funded scientists*

The percentage of the value of signed contracts across the different areas of scientific activity in the Project Tree, particularly of the value of contracts attributed to IARC, is similar to the percentage of Regular Budget funded staff assigned to those areas over the same period (Table 15). This again demonstrates broadly equivalent levels of productivity and success in obtaining external research funding across the areas. That being said it is recognized that some areas are less competitive for major traditional competitive grant funders, notably in relation to work on cancer registry development or training and capacity building.

Table 15: Average distribution of IARC staff in years 2016 to 2018 according to the main areas of the IARC Project Tree, compared to the value of extra-budgetary funding secured from Jan. 2016 to June 2018

Project Tree area	% all scientific staff (from Table 6 above)	Total value of signed contracts (from Table 12 above)	Total value attributed to IARC (from Table 12 above)
PT-1[1]	14.9%	1.89 (2.77%)	1.88 (7.59%)
PT-2[1]	60.9%	50.50 (73.97%)	15.84 (63.54%)
PT-3[1]	9.7%	9.91 (14.52%)	5.15 (20.66%)
PT-4[1]	14.4%	5.77 (8.45%)	1.86 (7.46%)

[1] Distribution of IARC Groups by Project Tree areas for the calculation of staff numbers:
PT-1 – CSU, *MPA*, *WCT*; PT-2 – ICB, ICE, ENV, BMA, NEP, GCS, GEP, EGE, MMB, IMO;
PT-3 – GHI, PRI, SCR, *IHB*; PT-4 – ETR, LSB, *BST*, *DEX*, *NMB.*
Figures are approximate as they do not reflect the fact that Groups have activities across several Project Tree areas; Groups that were dissolved or created during the reporting period are shown in italics.

2 INCREASING CAPACITY FOR CANCER RESEARCH

2.1 DEVELOPING HUMAN RESOURCES

2.1.1 Early Career and Visiting Scientists (ECVS)

2.1.1.1 *Mapping of ECVS at IARC and breakdown by category (PhD students, fellows, postdocs, Senior Visiting Scientists) by region/country*

2.1.1.2 *Mapping of IARC Postdoctoral Fellowships awarded by region/country*

2.1.1.3 *Proportion of ECVS and Postdoctoral Fellowships from LMICs*

Overall a total of 194 Early Career and Visiting Scientists (ECVS) (41 Doctoral Students, 43 Postdoctoral Fellows, 52 Postdoctoral Scientists, and 58 Visiting Scientists) from 52 different countries were hosted at the Agency during the reporting period (see Figure 5). In addition 135 trainees (Master/Batchelor students and Continuing Professional Development Trainees) also received training at the Agency.

64.9% of ECVS originated from IARC Participating States and 33.5% from LMICs. The large proportion of ECVS from Participating States is partly due to the large number of Doctoral Students and Postdoctoral Scientists from the host country, France, but even discounting these two groups the proportion of ECVS originating from other Participating States is still over 53%.

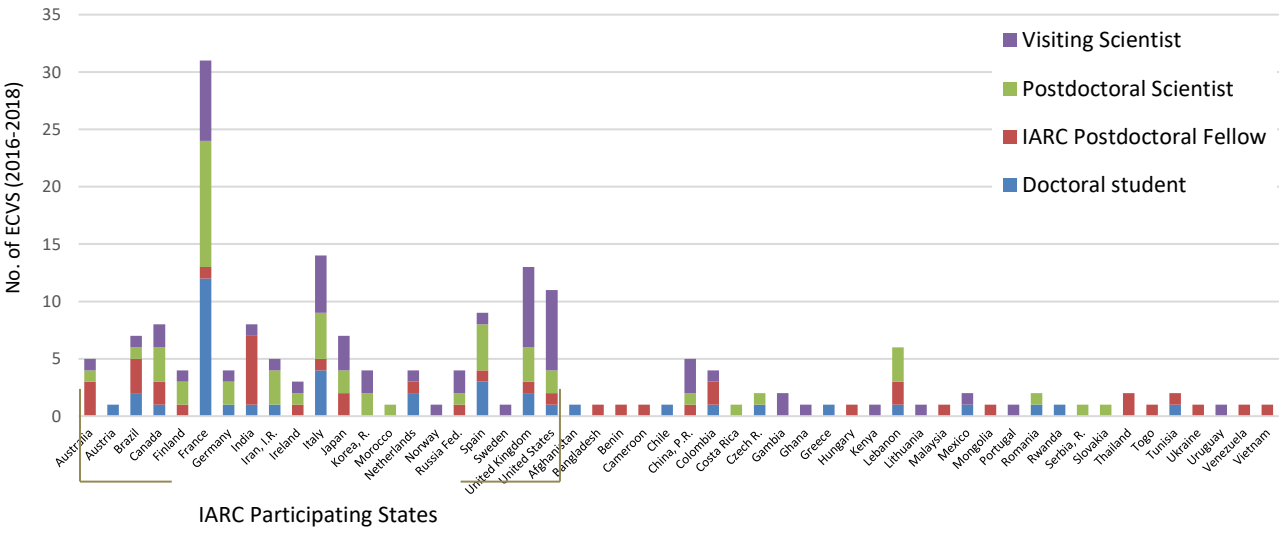


Figure 5: Mapping of Early Career and Visiting Scientists (ECVS) hosted at IARC from Jan. 2016 to June 2018 by type and by country (the category "Visiting Scientist" includes Senior Visiting Scientists and other visiting scientists with stays at IARC greater than 30 days).

Looking specifically at the IARC Fellowships, overall 43 Postdoctoral Fellows were hosted at IARC during the reporting period (i.e. already at IARC prior to 2016 plus newly awarded/extended), with the majority of Fellows originating from Participating States (58.1%) and from LMICs (73.2%) (see Table 16 and Figure 6). It should be noted that the IARC Postdoctoral Fellowship Programme was suspended in 2018 due to regular budget reductions, so no new awards were made that year and hence the drop in numbers.

Table 16: Number of IARC Fellows newly awarded/extended from Jan. 2016 to June 2018

Year	No. of IARC fellowships (new awards/2nd year renewals)[1]	No. of Fellows from LMICs
2016	17 (7 + 10)	10
2017	14 (7 + 7)	12
Jan-June 2018	7 (0 + 7)	6
Average[2]	12.7 (4.7 + 8)	9.3
Average previous MTS (2010–2015)	13.5 (9.8 + 7.3)	9.7

[1] Post-doctoral fellowships (new + second year renewals), including IARC-Australia and IARC-Ireland Fellows in 2013–2015

[2] Averages are calculated on the basis of three years of awards of IARC Fellowships

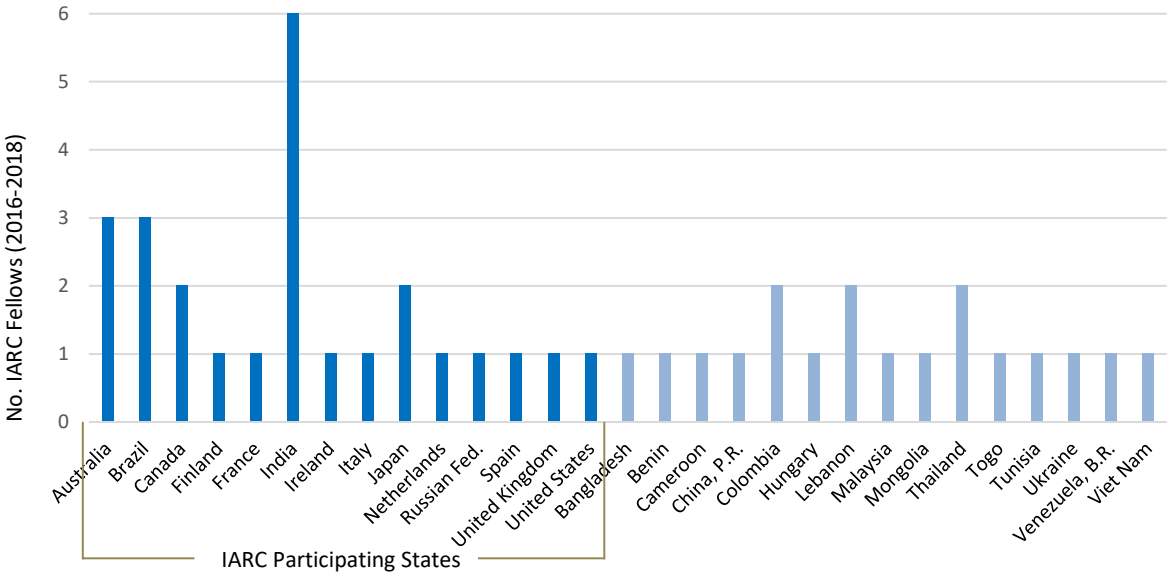


Figure 6: Mapping of IARC Fellows hosted at IARC from Jan. 2016 to June 2018 by country.

These figures clearly demonstrate the broad impact of the IARC ECVS training programme, which contributes to the development of the next generations of cancer researchers across the world, with a clear focus on training early career scientists from IARC Participating States and from LMICs.

2.1.2 IARC Courses

2.1.2.1 *Mapping of courses organized by region/subject*

2.1.2.2 *Proportion of courses held in LMICs*

2.1.2.3 *Total number of course participants by region/subject*

IARC training events include courses organized by the Education and Training Group (ETR), such as the *IARC Summer School on Cancer Epidemiology* held in Lyon, as well as specialized courses and workshops organized by the scientific Groups, often with support from ETR, in Lyon or with partners throughout the world.

Table 17: Number of courses organized by IARC from Jan. 2016 to June 2018

Year	No. courses organized	No. different countries	No. courses in LMICs	No. participants
2016	36	23	19	1410
2017	32	16	15	1324
Jan-June 2018	15	12	12	449
Average	32.7	21	19.3	1210.7
Average previous MTS (2010–2015)	13.7	8.8	7.2	456.3

The focus of the IARC Courses Programme remains on providing training in cancer research where it is most needed, with 79.5% of courses held in LMICs and 83.9% of course participants originating from these regions (see Figure 7).

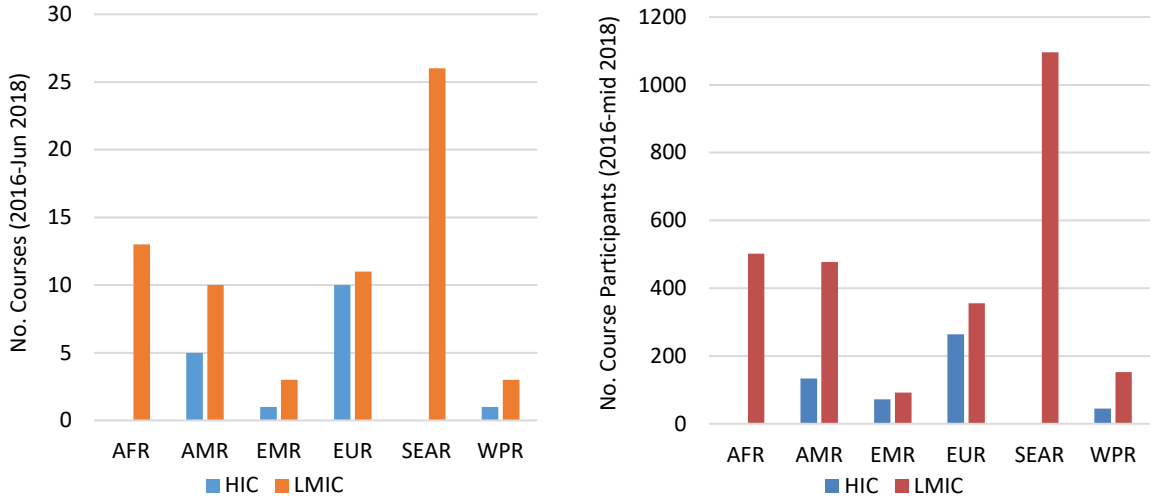


Figure 7: Mapping of IARC Courses by WHO Region and distribution of courses and course participants from high-income countries (HIC) and low- and middle income countries (LMICs).
(AFR – African Region; AMR – Americas Region; EMR – Eastern Mediterranean Region; EUR – European Region; SEAR – South-East Asia Region; WPR – Western Pacific Region).

There was a marked increase in the number of courses and attendants during the reporting period in relation to the previous MTS (see Table 17) due primarily to the development of capacity building initiatives such as GICR (cancer registration) and BCNet (biobanking), as well as an increase in e-learning events (i.e. online courses, webinar series, blended courses, etc.) made possible through the continued strengthening of the infrastructure for the production and dissemination of online learning material.

2.1.2.4 *Number of trainers trained (i.e. GICR, cancer screening, etc.)*

Data on this item could not be obtained from data currently available at the Agency – see instead case study #23 and also case studies #28 and #32, which are also relevant to this area.

2.1.3 Training Materials

2.1.3.1 *List of published training manuals, guidelines, etc*

The Agency has started to take advantage of courses and training to record lectures and make these available to a wider audience as a result. Examples of recorded lectures and webinars are provided below (Tables 18 and 19).

Table 18: Selection of recorded lectures

Screening Group
• Treatment of cervical precancerous lesions using thermocoagulation and cryotherapy (2016) http://video.iarc.fr/channelcatmedia/12/MEDIA161104140536797
Cancer Surveillance Section
• Cancer Surveillance and Registration (2017) http://video.iarc.fr/channelcatmedia/13/MEDIA170725161453668
Laboratory Services and Biobank Group
• Introduction to Biobanking - IARC-BCNet – BBMRI-ERIC Training in Biobanking for Pathologists and Pathology/Histology Technicians (2017) http://video.iarc.fr/videos/?video=MEDIA171002141731311 • BCNet Symposium 2017 (all presentations) http://bcnet.iarc.fr/projects/bcnet_symposium.php

Summer School 2017 State of the Art Lectures - Introduction to Cancer Epidemiology Module
• Obesity, Unhealthy Foods, Physical Inactivity and other Lifestyle Factors and Cancer Development http://video.iarc.fr/channelcatmedia/11/MEDIA170717155815669 • Occupation and Environmental Cancer http://video.iarc.fr/channelcatmedia/11/MEDIA170706120206626 • Genetic Epidemiology http://video.iarc.fr/channelcatmedia/11/MEDIA170706105058975 • Radiation and Cancer http://video.iarc.fr/channelcatmedia/11/MEDIA170705101558314 • Infection and Cancer http://video.iarc.fr/channelcatmedia/11/MEDIA170705101118349 • Diet and Cancer http://video.iarc.fr/channelcatmedia/11/MEDIA170704104932663 • Evaluation of Prevention Strategies for Cancer Control http://video.iarc.fr/channelcatmedia/11/MEDIA170704104341231 • Principles of Screening http://video.iarc.fr/channelcatmedia/11/MEDIA170703101233786

Table 19: Selection of webinar archives

Cancer Surveillance Section
• Survcan-3 - Data Collection for Survival Studies: follow-up using passive and active methods (2017) http://video.iarc.fr/channelcatmedia/13/MEDIA170315100511256 • GICR - TNM Esencial - Una herramienta para los registros de cáncer (2017) http://video.iarc.fr/channelcatmedia/13/MEDIA170821164009839
Laboratory Services and Biobank Group - B3Africa project
• Introduction to the eB3Kit Biobanking (2016) http://video.iarc.fr/videos/?video=MEDIA180417152947340 • Introduction to ELSI: The Need for Biobank and the Importance of ELSI Biobanking (2016) http://video.iarc.fr/videos/?video=MEDIA180417160041713 • Key Aspects of International Normative ELSI Perspectives on Biobanking (2016) http://video.iarc.fr/videos/?video=MEDIA180417160346801 • Presentation of the B3Africa Ethical and Legal Framework (2016) http://video.iarc.fr/videos/?video=MEDIA180417160802906 • Challenge Accessing and Sharing Bio-Ressources (2016) http://video.iarc.fr/videos/?video=MEDIA180417162035536 • Minimum Information About Data Sharing (MIABIS) (2016) http://video.iarc.fr/videos/?video=MEDIA180417162406510 • Introduction to Bioinformatics in the eB3Kit (2017) http://video.iarc.fr/videos/?video=MEDIA180417170201976 • Analysing Sample Data Using STATegra EMS (2017) http://video.iarc.fr/videos/?video=MEDIA180417170409945 • Material Transfer Agreements (2017) http://video.iarc.fr/videos/?video=MEDIA180417171138372 • Data Transfer and EU Data Protection Requirements (2017) http://video.iarc.fr/videos/?video=MEDIA180417171552370 • Mobile Data Collection - Part 1 and Part 2 (2018) http://video.iarc.fr/videos/?video=MEDIA180508160352215

2.1.3.2 *IARC Biobank Learning portal (2018) – http://biobanklearning.iarc.fr/*

Biobank Learning is an online platform for the dissemination of learning and training materials for biobank-based research professionals. It includes resources developed in the frame of the B3Africa project, the BCNet initiative as well as other relevant projects and initiatives. It also provides links to resources developed by other actors. The Biobank Learning portal will be sustained and further developed through the BCNet initiative.

2.1.3.3 *Number of purchases/downloads/views of published training materials*

Table 20: Number of downloads and visits of published training manuals from the IARC Screening website

Item	Number of downloads	Number of visits
Colposcopy and treatment of cervical intraepithelial neoplasia: a beginners' manual http://screening.iarc.fr/colpo.php	69 890	367 740
A practical manual on visual screening for cervical neoplasia http://screening.iarc.fr/viavili.php	5 074	89 454
Cytopathology of the uterine cervix - digital atlas http://screening.iarc.fr/atlascyto.php	N.A.	82 693
A digital manual for the early diagnosis of oral neoplasia http://screening.iarc.fr//atlasoral.php	N.A.	54 729
Histopathology of the uterine cervix - digital atlas http://screening.iarc.fr//atlashisto.php	N.A.	24 945
Atlas of Colposcopy – Principles and practice http://screening.iarc.fr//atlascolpo.php	N.A.	12 093
Breast self-examination (BSE) http://screening.iarc.fr//breastselfexamination.php	N.A.	405

Most of the resources listed in Table 20 were published before the reporting period, with the exception of "*Atlas of Colposcopy – Principles and practice*" published in 2017. They are included here to illustrate how key training resources produced by the Agency are accessed over time – see for example the large number of visits and downloads of "*Colposcopy and treatment of cervical intraepithelial neoplasia: a beginners' manual"*.

2.2 DEVELOPING NEW METHODOLOGIES

2.2.1 Number of downloads of IARC open access tools

Data on this item could not be obtained primarily because of the difficulty to define what constitutes an open access tool and partly because many of the websites are not amenable to our current approach to tracking download – see instead case studies #32 and #33.

2.3 DEVELOPING COLLABORATIVE NETWORKS

2.3.1 International collaboration networks

2.3.1.1 *Mapping of co-authorship of published papers*

The pattern of joint publications with other organizations represents a good proxy to analyse the coverage and magnitude of IARC's role in promoting international collaborative research. This is the first time the Agency has tried to capture and report on these parameters.

We commissioned a bibliometric analysis of IARC's publications network by one of the leading research groups in this area, the Centre for Science and Technology Studies (CWTS) at Leiden University, The Netherlands. The CWTS analyses focussed on the patterns of co-authorship of scientific publications at the levels of countries and organizations.

The analyses conducted were based on all "research articles" or "review articles" published by IARC from the period Jan. 2016 to April 2018[4], indexed in the Web of Science (WoS) database. Analyses were carried out on the complete set of 728 IARC papers published in this period, plus on a subset of 294 publications that were led by IARC scientists (i.e. in which IARC scientists had the first, last or corresponding author roles). Full details of the methodology and the results of the CWTS analyses can be found below.

The main analyses consisted of statistics on the number of IARC collaborative publications with different countries or organizations. The results presented were obtained with "fractional counting" which takes into account the total number of authors in a publication, reducing the weight of publications with large numbers of authors ("hyperauthorship publications") which would otherwise dominate the map of collaboration networks.

Figures 8 and 9 visualize the CWTS analyses of IARC's global network of collaborations. This was done both for collaborators at the country level (Figures 8a and 8b) and for collaborators at the organization level (Figure 9).

[4] The cut-off of April 2018, rather than June as in the rest of the report, was necessary to allow for data acquisition and completion of the analyses by CWTS in time for inclusion in this report.

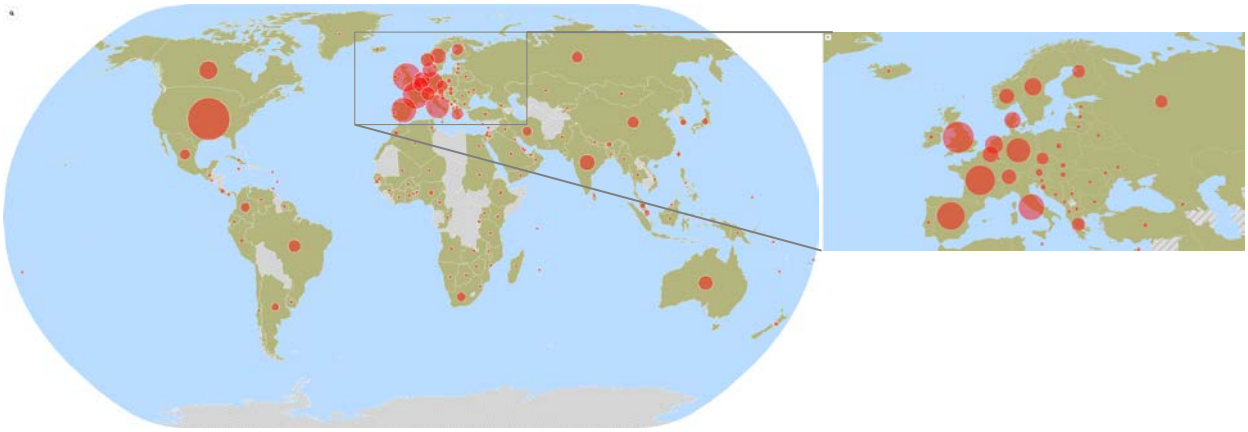


Figure 8a[5]: Map of IARC's research collaborations based on CWTS analyses of all joint publications for the period from Jan. 2016 to April 2018 corrected using fractional counting. The size of the circles represents the number of collaborations between IARC and all organizations in each country. Countries with whom IARC had no joint publications are shown in hashed colours. Data visualization created using FLOURISH* (https://flourish.studio/).

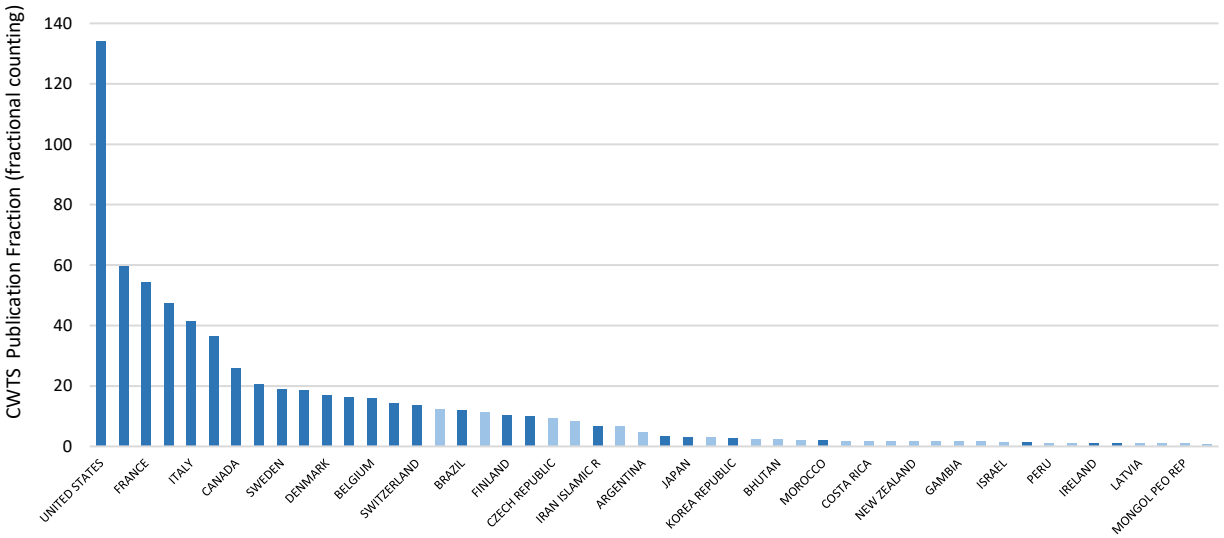


Figure 8b: Top 50 countries for IARC's research collaborations based on CWTS analyses of all joint publications for the period from Jan. 2016 to April 2018 corrected using fractional counting. Data for IARC Participating States is highlighted in dark blue.

[5] The boundaries shown on this and all the other maps in this report do not imply the expression of any opinion whatsoever on the part of IARC concerning the legal status of any country, territory, city or area of its authorities, or concerning the delimitation of its boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

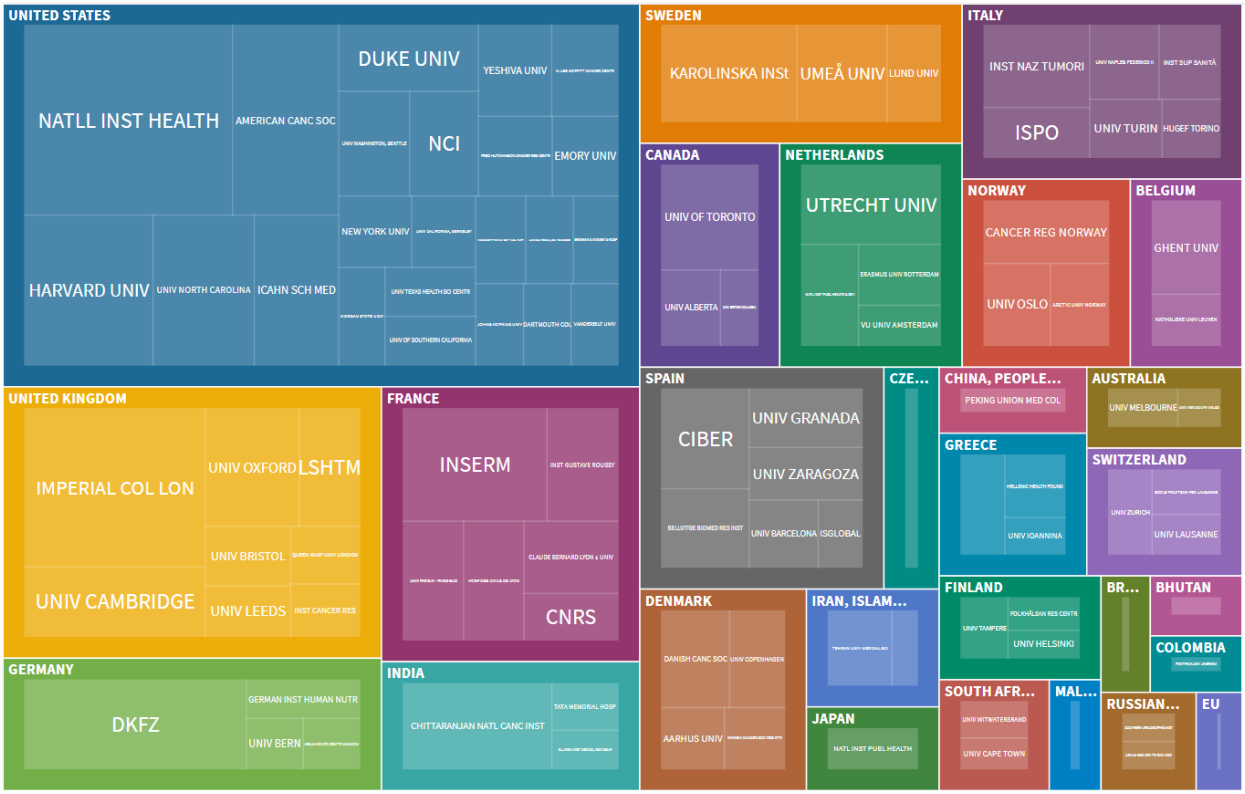


Figure 9: Treemap of IARC's research collaborations with other organizations based on CWTS analyses of all joint publications for the period from Jan. 2016 to April 2018 corrected using fractional counting. The size of the tiles represents the number of collaborations between IARC and each organization. Data visualization created using FLOURISH* (https://flourish.studio/).

The broad reach of IARC's global network of collaborations is evident from these results. Two features are particularly noteworthy: the first is the large number of countries (141/195 considering all publications and 101/195 considering only publications led by IARC) including many LMICs with whom IARC maintained active collaborations and published jointly over a period of only 2.5 years; the second is that a majority of IARC's collaborations, as assessed by joint publications, are with its Participating States (18 IARC Participating States ranked in the top 20 countries according to "all publications").

In a second set of analyses, CWTS calculated a series of standard bibliometric collaboration statistics for IARC and for a range of benchmarks (see Table 21). This provides the Governing Council with some comparison to other research organizations at national level.

The first benchmark consists of the combined publication output of five benchmark organizations based within IARC Participating States, in the period Jan. 2016 to April 2018. Benchmark organizations were selected amongst the top 50 organizations with most joint publications with IARC, which have a focus on cancer research and a publication output within the same order of magnitude[6].

The same statistics were calculated for three additional sets of benchmarks based on the top subject categories of IARC publications (see below).

Table 21: Collaboration statistics for the publications of IARC and of four benchmark sets of organizations and research subject categories.

	Avg. no. of organizations/ publication	Avg. No. of countries/ publication	% hyper-authorship/ publication	% articles with international collaborations
IARC	19.9	7.0	8.5%	93.1%
Benchmark organizations	11.4	3.4	3.6%	55.1%
WoS “Oncology” & “Public, Env. & Occup. Health”	3.1	1.4	0.1%	24.1%
CWTS top 9 meso-level areas	3.4	1.4	0.2%	24.0%
CWTS top 9 micro-level areas	3.9	1.6	0.5%	28.3%

The results for IARC are substantially higher across all bibliometric indicators of collaboration than those of the benchmark categories analysed. Of particular note are the IARC results for the “Average number of organizations per publication”, “Average number of countries per publication” and “Percentage of articles in which there are international collaborations” when compared to those of the group of benchmark organizations, which clearly demonstrate the focus on international research at the Agency.

[6] Search strategy for the selection of benchmarking organizations:

- Searched WoS Core Collection for ‘Organization enhanced’ – International Agency for Research on Cancer (IARC); Date range: 2008–2018 - Results: 4140 records
- Refined results by Organizations Enhanced; sorted by number of joint papers with other organizations; restricted to top 50; selected the organizations with a focus on cancer research
- Searched for total number of papers published by each organization in the same date range
- Selected those that have <5 times more publications than IARC
- 5 Selected
  - CATALAN INSTITUTE OF ONCOLOGY
  - FONDAZIONE IRCCS ISTITUTO NAZIONALE TUMORI MILAN
  - GUSTAVE ROUSSY
  - FRED HUTCHINSON CANCER CENTER
  - GERMAN CANCER RESEARCH CENTER DKFZ

2.3.1.2 *Mapping of international collaboration in the preparation of grant applications/successful grants*

In parallel with the analyses of joint publications shown above, the scientific networks involved in the preparation of grant applications present a useful additional dataset to illustrate IARC's role in promoting international collaborative research.

IARC personnel participated in the preparation and submission of 468 grant applications from January 2016 to June 2018, involving 539 individual scientists in 64 countries. During the same period 141 grants were signed, involving 441 individual scientists in 53 countries (see Table 22).

Table 22: Number of grants submitted or signed[1] from Jan. 2016 to April 2018 and number of external individual scientists who collaborated in their preparation

		IARC was a partner	**Coordinated by IARC**	**(%)**	**Total**	**External Partners**
2016	Submissions	65	113	(63%)	178	244
	Contracts signed	14	48	(77%)	62	293
2017	Submissions	59	128	(68%)	187	408
	Contracts signed	16	43	(73%)	59	118
Jan-Jun 2018	Submissions	36	67	(65%)	103	150
	Contracts signed	3	17	(85%)	20	67
Grand Total	**Submissions**	**160**	**308**	**(67%)**	**468**	**802[1]**
	Contracts signed	**33**	**108**	**(76%)**	**141**	**478[1]**

[1] These figures are higher than those quoted in the text as some of the external partners collaborated on the submission or signature of several grants in different years.

An interesting observation from these data is that the percentage of contracts signed is consistently about 10% higher for projects coordinated by IARC compared to all contracts submitted, suggesting that the success rate of applications is higher for projects coordinated by IARC.

The broad network of IARC collaborations is evident from the analysis of collaborations on research grants (Figure 10). Although the majority of collaborations on signed grants are again with IARC Participating States, the substantial number of grants signed with partners in LMICs is particularly noteworthy.

A comparison between the mapping of extrabudgetary funding (Figure 10) and publications (Figure 8a) reveals that IARC scientists collaborate with a far wider range of scientists in LMICs than would be expected from the funding profile alone. This at least partly reflects where funding sources are open to applications from IARC scientists. However, it also illustrates how the Agency brings resources, scientific cooperation and capacity building to many LMICs in Africa and parts of Asia. This is often achieved through a modest investment from the regular budget in the form of Collaborative Research Agreements or other forms of seed funding.

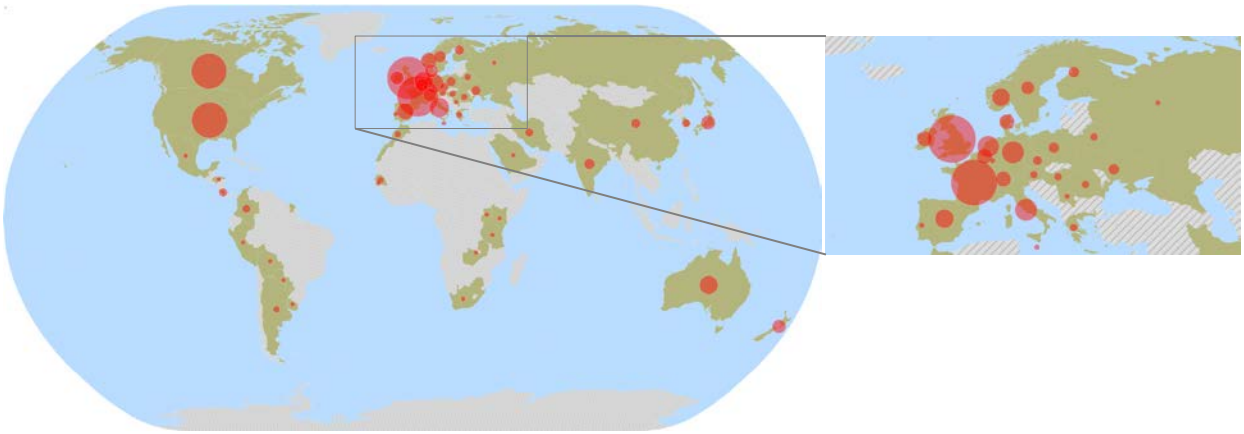


Figure 10: Map of IARC's collaborations based on research grants signed during the period from Jan. 2016 to April 2018. The size of the circles represents the number of collaborations between IARC and all organizations in each country. Countries with whom IARC had no joint grants signed during this period are shown in hashed colours. Data visualization created using FLOURISH* (https://flourish.studio/).

2.3.2 Management and participation in large international research consortia

Table 23: List of consortia led by IARC active during the period Jan. 2016 – June 2018

Consortium	Name	Focus area	IARC Role	No. of partners	No. of Countries
IACR	International Association of Cancer Registries	Cancer Registration	Coordinator	539	129
ACCIS	Automated Childhood Cancer Information System	Childhood Cancer	Coordinator	100	29
ILCCO	International Lung Cancer Consortium	Lung Cancer	Coordinator	79	25
AGRICOH	AGRICOH: A Consortium of Agricultural Cohort Studies	Pesticides and Cancer	Coordinator	29	12
SURVCAN	Cancer Survival in Africa, Asia, the Caribbean and Central America	Cancer Registration	Coordinator	27	14
CLIC	The Childhood Leukemia International Consortium	Childhood Cancer	Coordinator	26	12
EPIC	The European Prospective Investigation into Cancer and Nutrition	Nutrition and Cancer	Coordinator	23	10
GICR	Global Initiative for Cancer Registration Development	Cancer Registration	Coordinator	23	6
ARCAGE	Alcohol-related cancers and genetic susceptibility in Europe	Alcohol and Cancer	Coordinator	22	12
Interphone	Interphone study	Mobile Phones	Coordinator	17	14
EPI-CT	International Paediatric CT Scan	Medical Radiation and Cancer	Coordinator	17	11

Table 23: List of consortia led by IARC active during the period Jan. 2016 – Jun. 2018 (continued)

Consortium	Name	Focus area	IARC Role	No. of partners	No. of Countries
ESTAMPA	Multicentric study of cervical cancer screening and triage with Human papillomavirus testing	Cervical Cancer	Coordinator	13	8
BCNet	Biobank and Cohort Building Network	Biobank in LMICs	Coordinator	11	7
Synergy	Pooled analysis of European Case-Control Studies on the Interaction of Occupational Carcinogens in the Development of Lung Cancers	Lung Cancer	Coordinator	10	7
interCHANGE	International Consortium on Head and Neck Cancer Genetic Epidemiology-	Head and Neck Cancer	Coordinator	9	4
HPVC3	HPV cancer cohort consortium	HPV and Cancer	Coordinator	9	4
CPE	Cancer Prevention Europe	Cancer Prevention Coordination	Coordinator	9	6
ABC-DO	African Breast Cancer Research Network - Disparities in Outcomes	Breast Cancer	Coordinator	8	8
PRECAMA	Molecular subtypes of premenopausal breast cancer in Latin American women	Breast Cancer	Coordinator	5	5
ESCCAPE	Esophageal Squamous Cell Carcinoma Africa Prevention Research network	Esophageal Cancer	Coordinator	2	2

Table 24: List of consortia in which IARC is a partner, active during the period Jan. 2016 – June 2018

Consortium	Name	Focus area	IARC Role	No. of partners	No. of Countries
ENCR	The European Network of Cancer Registries	Cancer Registration	Partner	176	38
INHANCE	International Head and Neck Cancer Epidemiology Consortium	Head and Neck Cancer	Partner	77	27
OncoArray Consortium	A Network for Understanding the Genetic Architecture of Common Cancers	Cancer Genetics	Partner	49	10
iPAAC	Innovative Partnership for Action Against Cancer	Cancer Prevention Coordination	Partner	44	24
INTEGRAL	Integrative Analysis of Lung Cancer Etiology and Risk Consortium for Early Detection of Lung Cancer	Lung Cancer	Partner	32	12
ATBC	Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study	Vitamin and Cancer	Partner	27	6
CHANCES	Consortium on Health and Ageing: Network of Cohorts in Europe and the US	Ageing	Partner	17	9
NORDTEST	Parental Occupational Exposure to Organic Solvents and Testicular Germ Cell Tumors in their Offspring	Testicular Cancer	Partner	13	6
LYriCAN	LYon Recherche Innovation contre le CANcer	Cancer Treatment	Partner	9	1
SEMI-NUC	Prospective cohort study of residents near the Semipalatinsk nuclear test site	Radiation and Cancer	Partner	8	6
TRICL	Transdisciplinary Research for Cancer of Lung	Lung Cancer	Partner	8	4

Consortium	Name	Focus area	IARC Role	No. of partners	No. of Countries
COSMOS	International prospective cohort study of mobile phone users and health	Mobile phones	Partner	6	6
STOP	Science and Technology in childhood Obesity Policy	Nutrition and Obesity	Third-Party	29	15
BBMRI-ERIC	Biobanking and Biomolecular Resources Research Infrastructure	Biomedical	Observer	20	20
I4C	The International Childhood Cancer Cohort Consortium	Childhood Cancer	Supporting Agency	18	10
ANCR	Association of the Nordic Cancer Registries	Cancer Registration	Collaborator	9	5

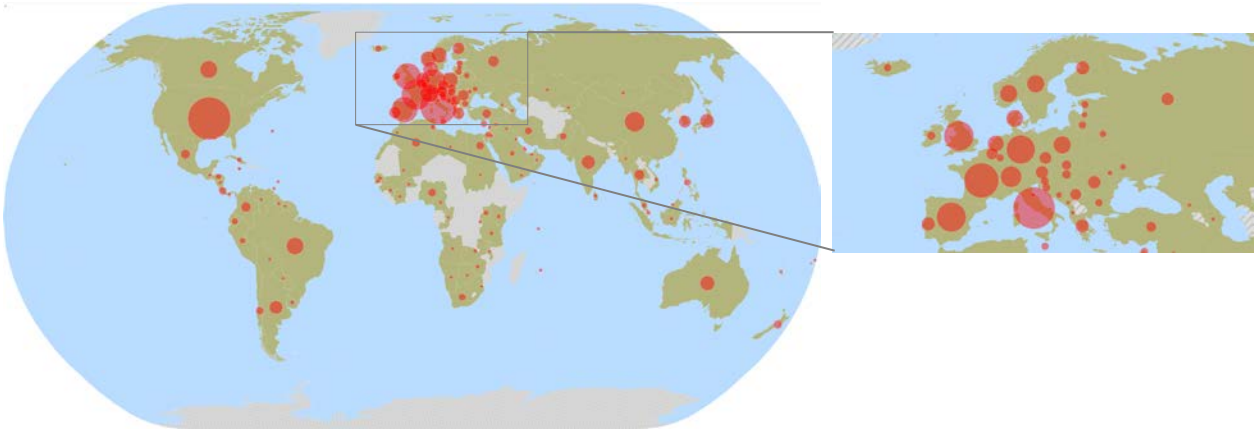


Figure 11: Map of IARC's collaborations based on research consortia active during the period from Jan. 2016 to June 2018. The size of the circles represents the number of collaborations between IARC and all organizations in each specific country. Countries with whom IARC had no collaborations based on research consortia during this period are shown in hashed colours. Data visualization created using FLOURISH* (https://flourish.studio/).

This is the first time that IARC has tried to capture data on the full range of consortia which it either leads or participates in. The data reveal the scale of IARC's influence and reach via these often complex and geographically diverse networks of researchers working across national boundaries. The summary data illustrate the confidence placed in IARC and its scientists by the international research community.

In Table 23 there is a list of 20 consortia which IARC scientists coordinate. These include a total of 978 partner institutions. The International Association of Cancer Registries (IACR) is of course an exception in comprising 539 partners to this total. It is this longstanding commitment to the Association that has enabled IARC to remain the go-to organization for global cancer statistics and for capacity building and cancer registry development.

Even without the contribution of the IACR there are 439 partners across 19 different consortia, which cover the full spectrum of IARC's MTS objectives in terms of research into cancer occurrence, causes, prevention, capacity building and shaping the international cancer research agenda.

In addition to leading these 20 consortia, IARC participates in a further 16 collaborative consortia comprising 542 partner organizations.

The figures for the total number of countries with whom IARC collaborates in the context of international research consortia are remarkably similar to those obtained in the bibliometric analyses (129/195 and 141/195 respectively).

The overall picture is one of broad reach consistent with IARC's mandate to promote international collaboration in cancer research.

2.4 DEVELOPING RESEARCH INFRASTRUCTURE

2.4.1 Support to the development of research infrastructures

2.4.1.1 *List of research platforms to which IARC provided support (by type of activity and type of support) [including the option of case studies]*

2.4.1.2 *Mapping of site visits on cancer registries [including the option of case studies]*

Data on these items could not be obtained because the data are not routinely captured and in the first case there is as yet no definition of what would constitute a research platform – see instead case studies #21, #22, #23 and #28.

3 PROVIDING STRATEGIC RESEARCH LEADERSHIP – SHAPING THE INTERNATIONAL CANCER RESEARCH AGENDA

3.1 DEVELOPING INSTITUTIONAL PARTNERSHIPS

3.1.1 Institutional agreements

3.1.1.1 *Mapping of MoUs, MoAs, CRAs, etc*

Table 25: Number of institutional agreements (Memorandum of Understanding, Memorandum of Agreement, Collaborative Research Agreement) signed during the period Jan. 2016 to June 2018

	Memorandum of Understanding	Memorandum of Agreement	Collaborative Research Agreement
No. of agreements signed	12	13	148
No. of institutions	10	13	130
No. of countries	9	11	42

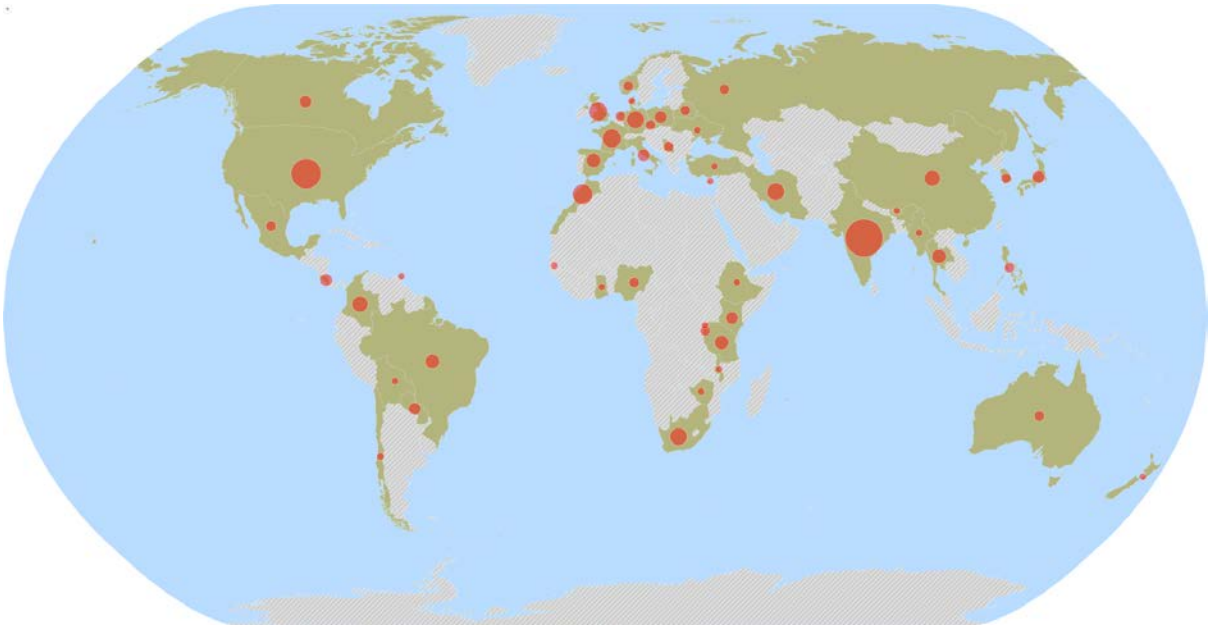


Figure 12: Map of IARC's institutional partnerships (MoUs, MoAs and CRAs) signed during the period from Jan. 2016 to June 2018. The size of the circles represents the number of agreements between IARC and all organizations in each specific country. Countries with whom IARC signed no agreements during this period are shown in hashed colours. Data visualization created using FLOURISH* (https://flourish.studio/).

The Agency signs formal agreements with many organizations through Memoranda of Understanding (typically at institution level), Memoranda of Agreement (typically at Department and Section level) or Collaborative Research Agreements (CRAs) related to specific projects. The assessment of CRAs (Table 25, Figure 12) shows the large number of formal collaborative arrangements into which the Agency enters with researchers across the world. These CRAs may include funds being transferred from IARC to collaborating partners or may simply provide the collaborative and legal framework within which the work can take place.

3.2 COMMUNICATION OF KEY ACTIVITIES TO STAKEHOLDERS AND THE PUBLIC

3.2.1.1 *Number of visits to IARC websites*

Table 26: Visitors to main IARC websites from Jan. 2016 to June 2018

	IARC Home page		Monographs		GLOBOCAN	
	Total visitors	Total visits	Total visitors	Total visits	Total visitors	Total visits
2016	451 330	606 772	293 688	424 663	274 527	486 743
2017	513 309	664 470	261 410	401 447	282 792	479 618
Jan-June 2018	191 496	258 443	139 440	208 349	156 416	254 245
Average	449 210	596 042	277 993	414 269	290 050	491 617
Average[1] 2011–2015	410 933	582 411	205 895	321 021	203 634	359 001

Visitor: A user that visits a given site. The initial session by an individual user during any given date range is considered to be an additional visit and an additional visitor. Any future sessions from the same user during the selected time period are counted as additional visits, but not as additional visitors.

Visit: The number of times a visitor has been to the site (number of individual sessions initiated by all visitors). If a user is inactive on the site for 30 minutes or more, any future activity will be attributed to a new session.

[1] Data not available for 2010

3.2.1.2 *Volume of downloads*

Table 27: Most popular downloads from IARC and Monographs websites (ranked by 2018 data and compared to 2017 and 2016 figures)

Item	Downloads		
	Jan-June 2018	2017	2016
Monographs 100E: Personal Habits and Indoor Combustions	116 048	N.A.	N.A.
IARC Monographs Classification List	86 820	167 707	165 424
Monograph Supplement 7: Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs Volumes 1 to 42	78 215	181 170	66 295
Cancer Epidemiology: Principles and Methods	70 307	153 106	213 533
IARC Handbook of Cancer Prevention Volume 8: Fruit and Vegetables	56 943	98 966	62 212
Monograph Volume 100C: Arsenic, Metals, Fibres, and Dusts	54 251	120 121	81 550
Press Release 240: IARC Monographs evaluate consumption of Red Meat and Processed Meat *(announced on 26/10/2015)*	47 898	117 840	187 176
Monograph Volume 82: Some Traditional Herbal Medicines, Some Mycotoxins, Naphthalene and Styrene	32 028	65 903	62 402

Item	Downloads		
	Jan-June 2018	2017	2016
"Blue Book" Pathology and Genetics of Tumours of the Digestive System – Third Edition	31 237	63 662	81 180
Monograph Volume 99: Some Aromatic Amines, Organic Dyes, and Related Exposures	26 578	73 346	66 552

The figures on the number of visitors to the most popular IARC websites during the reporting period (Table 26) show a steady progression across the board compared to the previous MTS.

The progression in the number of visitors is particularly noteworthy for the Monographs and GLOBOCAN websites reflecting the interest from the public and the scientific community in these IARC resources. This is also evident in the most popular downloads from the Agency's websites (Table 27) where seven of the 10 top downloads relate to the Monographs evaluations.

3.2.1.3 *Additional communication indicators (Altmetrics) both in traditional media and in new media*

It was not possible to obtain data on this area from ALTMETRICS (see above).

4 PROVIDING STRATEGIC RESEARCH LEADERSHIP – ENABLING AND SUPPORTING THE EFFICIENT CONDUCT AND COORDINATION OF RESEARCH

4.1 ENSURING THE EFFICIENT MANAGEMENT OF RESEARCH ACTIVITIES

4.1.1.1 *Compliance with the International Public Sector Accounting Standards (IPSAS) standards*

4.1.1.2 *Number of outstanding audit recommendations*

IARC fully implemented the International Public Sector Accounting Standards (IPSAS) since 1 January 2012. The Agency's IPSAS compliance has been reconfirmed by the external auditor each year including in 2016 and 2017. The same opinion is expected for the 2018 audit, whose outcome will be known in March 2019. Table 28 below summarizes the number of audit recommendations.

Table 28: Number of outstanding audit recommendations (at end-November 2018)

Year	Total audit recommend.	Implemented audit recommend.	Outstanding audit recommend.
2010-2011[1]	6	6	-
2012	6	6	-
2013	10	10	-
2014	11	11	-
2015	7	7	-
2016	6	6	-
2017	4	2	2
Total	**44**	**42**	**2**

[1] Prior to IPSAS implementation, the financial statements as well as the audit were prepared on a biannual basis

4.1.1.3 *Compliance with the Project Management Institute/ WHO Project Management Centre of Excellence (PMCE) standards*

It was not possible to include data on the compliance with Project Management Institute (PMI) standards as the WHO project to measure compliance has changed direction. Instead, WHO established a Project Management Centre of Excellence (PMCE), and invited IARC to participate. The project management methodology applied at IARC is based on international best practices, i.e. PMI and PMCE2 standards, adapted to IARC's needs.

C. CASE STUDIES

Table of contents:

Case Study #1: HPV VACCINATION – INFORMING WHO RECOMMENDATIONS FOR LESS THAN THREE DOSES

MTS areas: These studies contribute to IARC MTS Project Tree objective 3.1.1, 3.2.1, 4.1.1 and 4.2.2

- 3.1.1 Analyse the effectiveness of primary cancer prevention strategies
- 3.2.1 Identify factors influencing the effective implementation of primary and secondary prevention programmes
- 4.1.1 Award fellowships and provide training through participation in collaborative research projects
- 4.2.2 Improve and implement laboratory methods

IARC Sections/Groups involved: led by Screening (SCR) and Prevention and Implementation (PRI), with contributions from Infections and Cancer Biology (ICB)

The prophylactic vaccines against human papillomavirus (HPV) were initially recommended to be administered in three doses based on the results of the pre-licensure phase III efficacy trials. The robust and durable antibody response against the targeted HPV types and the stronger immune response observed in adolescent girls compared to the adult phase III trial subjects provided the justification to evaluate the efficacy of less than three doses of the vaccine in adolescent girls. A reduced number of doses will not only reduce the cost of the vaccine and of its administration but also simplify the logistics of implementation of the vaccination programmes.

A study coordinated by IARC in India initiated in 2009 is following nearly 15 000 girls who received either 3, 2 or a single dose of the quadrivalent HPV vaccine at 10-18 years if age. The preliminary results of this study demonstrated that 100% of the girls receiving two doses sero-converted and the serum antibody titre and antibody avidity were non-inferior to that in the recipients of three doses.

IARC also contributed to the Costa Rica HPV Vaccine Trial sponsored by the US National Cancer Institute, a phase III pre-licensure clinical trial of the bivalent HPV vaccines in which 7 466 women (aged 18-25 years) were randomized to receive either two doses or a single dose of the HPV vaccine or a control (hepatitis A vaccine). The HPV antibody levels measured at one month following the initial dose, and the four-year efficacy against persistent HPV 16 or 18 infections among women who were HPV DNA negative at the time of vaccination were not significantly different irrespective of the number of doses received[1,2].

The results of these studies have had a major impact, contributing significantly to the evidence-base supporting the decision by WHO's Strategic Advisory Group of Experts (SAGE) on HPV vaccination to recommend only two doses of the vaccine for girls below 15 years of age[3].

The high efficacy of a single dose of vaccine to protect against persistent vaccine-targeted HPV infection observed in these studies encouraged further investigations into the efficacy of a single dose of HPV vaccine. IARC is a key collaborator in the recently initiated NCI sponsored randomized trial to evaluate efficacy of single dose of bivalent and nonavalent vaccines in Costa Rica (ESCUDDO trial).

The most recent results of the Indian study further demonstrate the non-inferiority of immunogenicity and efficacy against persistent infections in girls vaccinated at 15-18 years of age compared to those vaccinated at an earlier age. Furthermore, the ongoing follow up of the participants beyond seven years demonstrated that the recipients of single dose of the HPV vaccine have comparable high level of protection to those seen in the recipients of three or two doses.

The Indian and the Costa Rican trials are expected to provide adequate evidence to the WHO SAGE to support extending the two dose recommendation to 15-18 year old girls and to decide on the efficacy of single dose of the HPV vaccines. These projects improved the research capacities in the implementing countries through successful technology transfer to perform HPV immunological assays and genotyping tests.

Barshi, India – August 2017

Barshi, India – August 2017

Figure – HPV vaccination and follow-up of 10–18 years old girls in India

References

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3. WHO. Immunization, Vaccines and Biologicals. Documentation from previous SAGE meetings. 2018. Available from: http://www.who.int/immunization/sage/previous/en/index.html

Case Study #2: DEVELOPING QUALITY ASSURANCE GUIDELINES FOR CANCER SCREENING PROGRAMMES IN THE EUROPEAN UNION AND REPORTING ON THE STATUS OF PROGRAMME IMPLEMENTATION

MTS areas: These activities contribute to IARC MTS Project Tree objective 3.1.2, 3.2.1, 5.3.1 and 5.4.1

- 3.1.2 Analyse the effectiveness of secondary cancer prevention strategies
- 3.2.1 Identify factors influencing the effective implementation of primary and secondary prevention programmes
- 5.3.1 Create and maintain key strategic partnerships with national, regional and international organisations
- 5.4.1 Effectively communicate and disseminate the work of the Agency

IARC Sections/Groups involved: led by Screening (SCR) with contributions from Cancer Surveillance Section (CSU) and Prevention and Implementation (PRI)

The Health Ministers of the European Union (EU) unanimously adopted a set of recommendations in December 2003 to implement breast, cervical and colorectal cancer screening programmes through a systematic population-based approach with appropriate quality assurance. The recommendations called for the development of best practice guidelines in cancer screening and the periodic submission of a status report to the European Council on programme implementation in the EU member States.

IARC was selected to lead the preparation of the status reports on the progress of implementation of cancer screening programmes in the EU member States in 2007[5] and again in 2017[3], developed under the framework of the European Partnership for Action Against Cancer (EPAAC). IARC provided the secretariat for this project, working along with the Reference Centre for Epidemiology and Cancer Prevention in Piemonte and the Finnish Cancer Registry to coordinate the contributions from nearly 100 programme managers and other experts closely involved with the cancer screening programmes of their respective countries. This work builds upon the expertise gained by IARC in leading the preparation of the European Guidelines for Quality Assurance in Breast[2], Cervical[1] and Colorectal[4] cancer screening, coordinating the inputs from a large number of experts from within and outside Europe. IARC also contributes the scientific evidence-base for screening through the production of Handbooks on Cancer Prevention (cervical, breast and colorectal cancers having been covered, with an update on cervical cancer envisaged).

The published guidelines and reports were made freely accessible online through the European Commission (EC) and the IARC website. The EC submitted the screening reports to the Ministries of Health of all the member states, and the key findings were presented at the meetings of Experts on Oncology from the EU and the European Cancer League.

The evidence-based guidelines prepared by IARC formed the framework to guide EU member States to introduce or improve their cancer screening programmes with appropriate quality standards. They also reduced the disparities within and among the member States in the quality of care in screening, diagnosis and treatment. The two status reports on cancer screening

prepared by IARC highlighted the substantial progress made within a decade in the EU to roll-out population-based screening for breast (implemented in 25 countries in 2016 compared to 22 in 2007), cervical (implemented in 22 countries in 2016 compared to 17 in 2007), and colorectal (implemented in 23 countries in 2016 compared to 12 in 2007) cancers. The second report identified a set of core performance indicators that successfully reflect the balance between best practices and the diverse socio-cultural and economic backgrounds of the EU member States.

This project illustrates IARC's contributions to evaluating scientific evidence to improve cancer control programmes and support policy development at national level. The updated guidelines for cancer screening are relevant beyond Europe. The well-standardized quality assurance indicators and their benchmarks included in the second screening report can be used by screening programmes of countries worldwide. Based on the success of the evaluation of EU screening programmes and leveraging the huge network of experts created through the project, the IARC Screening Group launched a new project 'Cancer Screening in Five Continents' (CanScreen5), which aims to collect information in a harmonized manner on the characteristics and performance of cancer screening programmes across the globe and disseminate this information to improve programme management, inform policy making and support research.

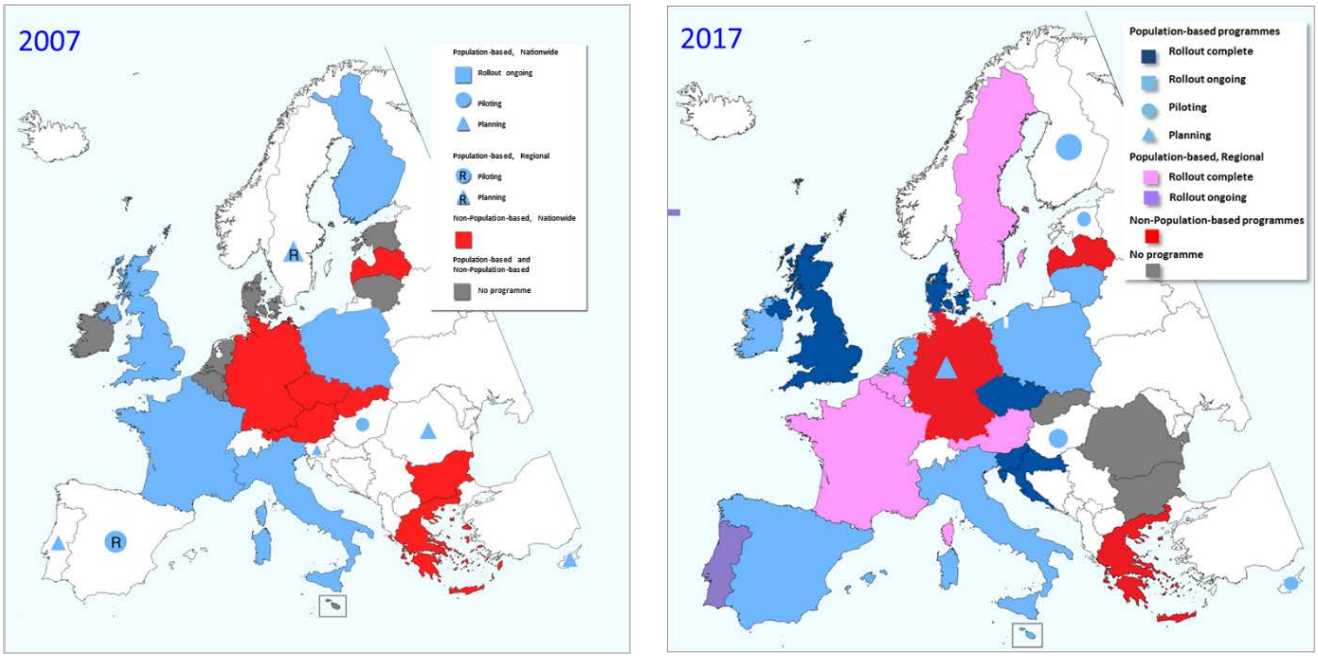

Figure – Progress in status of implementation of colorectal cancer screening programmes in the European Union member States

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Case Study #3: WHO TOBACCO KNOWLEDGE SUMMARY: TOBACCO & CANCER TREATMENT OUTCOMES

MTS areas: These activities contribute to IARC MTS Project Tree objectives 3.1.3, 3.2.1 and 5.4.1

- 3.1.3 Enhance understanding of the factors affecting cancer prognosis
- 3.2.1 Identify factors influencing the effective implementation of primary and secondary prevention programmes
- 5.4.1 Effectively communicate and disseminate the work of the Agency

IARC Sections/Groups involved: Environment and Radiation Section (ENV)

Worldwide, more than 1.1 billion people smoke tobacco and at least 367 million people use smokeless tobacco. Tobacco use is a major cause of cancer (IARC Monographs Vol. 100E, 2012) and a substantial proportion of users will continue to use, or relapse after a brief attempt at quitting, even after a diagnosis of cancer. Although tobacco users with cancer may be well aware of tobacco-related health risks, cessation of tobacco use remains challenging because of its addictiveness.

It is important for both tobacco users with cancer and the health-care providers treating them to know whether, and to what extent, continuation or cessation of tobacco use after a diagnosis might affect cancer treatment outcomes. This knowledge may influence the level of support that patients may seek, or their health-care providers organize, to help cancer sufferers quit.

The WHO Tobacco Knowledge Summaries are a programme of WHO Prevention of Noncommunicable Diseases' (PND) Tobacco Free Initiative (TFI) which aims to summarize the current evidence on tobacco and various disease and public health issues. They are intended as an advocacy tool to widely include the public and health care professionals from various fields in the fight for tobacco control and prevention of tobacco-related diseases.

IARC, in collaboration with WHO, produced the summary on tobacco consumption and cancer treatment outcomes[1] with the aim of informing oncology care providers about the current evidence on tobacco use by cancer patients and its effect on treatment outcomes and to encourage them to incorporate tobacco cessation support into standard oncology care.

IARC conducted a comprehensive search and review of studies on the associations between continued tobacco use vs. cessation following cancer diagnosis and cancer treatment outcomes, with additional weight given to systematic reviews and original studies published after the most recent systematic reviews. The outcome was that although the body of evidence that specifically addresses risks related to continuing smoking as opposed to cessation following a cancer diagnosis is limited, the existing data support the conclusion that continued smoking interferes with cancer treatment and worsens treatment outcomes. It further concluded that by quitting smoking, cancer patients have the potential to improve their treatment outcomes.

Despite the above evidence, support for the cessation of tobacco consumption is currently lacking in most clinical oncology settings. Further action promoting and supporting tobacco cessation is needed in order to reduce an avoidable burden of morbidity and premature mortality in cancer patients.

The dissemination of this Tobacco Knowledge Summary on tobacco consumption and cancer treatment will raise awareness among oncology care providers and cancer patients about this additional adverse health effect of tobacco use and promote the introduction tobacco control initiatives in the oncology setting. Furthermore, this work is expected to contribute to one of the policy goals of the WHO Framework Convention on Tobacco Control, on the introduction of programmes supporting tobacco consumption cessation into all health-care systems, so that all tobacco users can be identified and offered support, particularly after a cancer diagnosis.

Figure – WHO Tobacco Knowledge Summary: Tobacco & Cancer Treatment Outcomes

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[1]International Agency for Research on Cancer (IARC), [2]World Health Organization (WHO), [3]The University of Newcastle Australia
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Available from:
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Case Study #4: IARC MONOGRAPHS AND HANDBOOKS ON TOBACCO CONTROL

MTS areas: These activities contribute to IARC MTS Project Tree objectives 2.3, 3.3 and 5.4

2.3 Provide expert evaluations of the available evidence-base to identify human carcinogens

3.3 Provide expert evaluations of the available evidence-base in order to recommend prevention strategies

5.4 Effectively communicate and disseminate the work of the Agency

IARC Sections/Groups involved: IARC Monographs (IMO) and IARC Handbooks (IHB)

The imperative to curb the global tobacco epidemic has been a prime objective of the WHO and of the Agency, with the *IARC Monographs* producing several volumes evaluating the carcinogenicity of tobacco products. In 2002, a re-evaluation of the evidence on the carcinogenicity of tobacco smoking (*Monograph* Vol. 83) revealed the ever-expanding spectrum of tobacco-related cancers. A particularly important outcome of this *Monograph* was the evaluation of second-hand tobacco smoke as Group 1 carcinogen, leading to smoking bans in public spaces in many countries worldwide. This *Monograph* was also instrumental in paving the way for the WHO Framework Convention on Tobacco Control (WHO FCTC), which was adopted by the World Health Assembly in May 2003 and entered into force in February 2005. A few years later the use of smokeless tobacco (*Monograph* Vol. 89) was also confirmed as a Group 1 carcinogen, based primarily on data from South-East Asia and countries with migrant populations of this region.

In 2006 the *IARC Handbooks of Cancer Prevention* introduced tobacco control as an area of focus for their reviews and evaluations. *Handbook* Vol. 11, following up on *Monograph* Vol. 83, concluded on the substantial reversal of risk of cancer and other chronic diseases after smoking cessation. By 2011 the *IARC Handbooks* had published three more volumes on tobacco control, addressing the impact of interventions at the societal level to reduce tobacco use (Vol. 12-14). *Handbook* Vol. 12 presents a comprehensive framework for guiding the evaluation of tobacco control policies proposed in the WHO-FCTC, aimed at informing policy-makers in the 181 countries presently subscribers to the Convention. This volume was followed by evaluations of the effectiveness of smoke-free policies (Vol. 13), and of tobacco tax and price interventions in controlling tobacco use (Vol. 14) (Article 6 of the WHO-FCTC). IARC was invited to present the results of the evaluation on taxation and price policies in tobacco control to the WHO FCTC shortly after.

In reviewing the evidence, the *Handbooks* also identified data gaps and research needs. For instance, most evidence from *Handbooks* Vol. 11, 13 and 14 comes from high-income countries and is on cigarette/tobacco smoking. There are obvious research gaps on smokeless tobacco, and corresponding gaps in FCTC-based tobacco control activities. Some of these gaps were addressed through a collaboration between IARC, WHO SEARO, the Indian Ministry of Health, and the US National Cancer Institute, which resulted in a joint policy paper from SEARO submitted for publication.

The impact of the *Monographs* and *Handbooks* has been critical for the global fight against tobacco, by providing solid evidence driving the development and implementation of policy on tobacco control both at the national and supranational levels. Future *Handbooks* evaluating the effectiveness of risk reversal, and taxation and price policies for smokeless tobacco, as well as plain packaging for tobacco products, will represent an important addition to the fight against the tobacco epidemic.

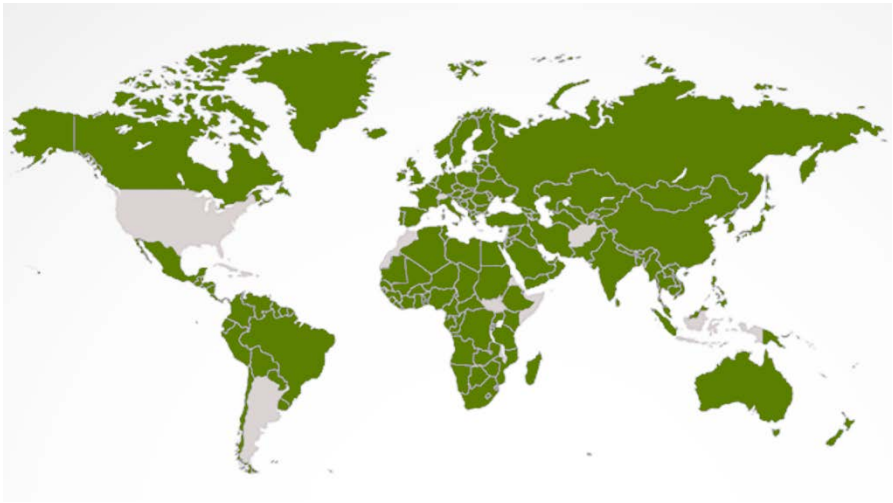


Figure – Map showing countries that have ratified the FCTC treaty (in green), December 2018. Source: http://www.who.int/fctc/cop/fr/

Case Study #5: IMPACT OF THE IARC WORKING GROUP REPORT VOL. 1 AND IARC MONOGRAPH 100D ON RECOMMENDATIONS ON ARTIFICIAL TANNING DEVICES

MTS areas: These activities contribute to IARC MTS Project Tree objectives 2.3 and 5.4

2.3 Provide expert evaluations of the available evidence-base to identify human carcinogens

5.4 Effectively communicate and disseminate the work of the Agency

IARC Sections/Groups involved: IARC Monographs (IMO)

Melanoma of the skin is a common cancer in many high-income countries, where it ranks 9th in terms of incidence. More broadly, an estimated 89% of all cancers attributable to ultraviolet (UV) radiation exposure occur in very-high HDI countries (GLOBOCAN 2018). The fact that exposure to UV radiation is the primary risk factor for skin melanoma makes this cancer easily preventable.

Solar radiation is the main source of human exposure to UV radiation, and the causal association between exposure to solar radiation and all major types of skin cancer has long been established and documented by the *IARC Monographs*[1]. Another important source of UV radiation, particularly in developed countries, comes from the use of UV-emitting tanning devices. Powerful tanning equipment may deliver exposures to UV radiation 10-15 times as intense as midday sunlight on the Mediterranean Sea.

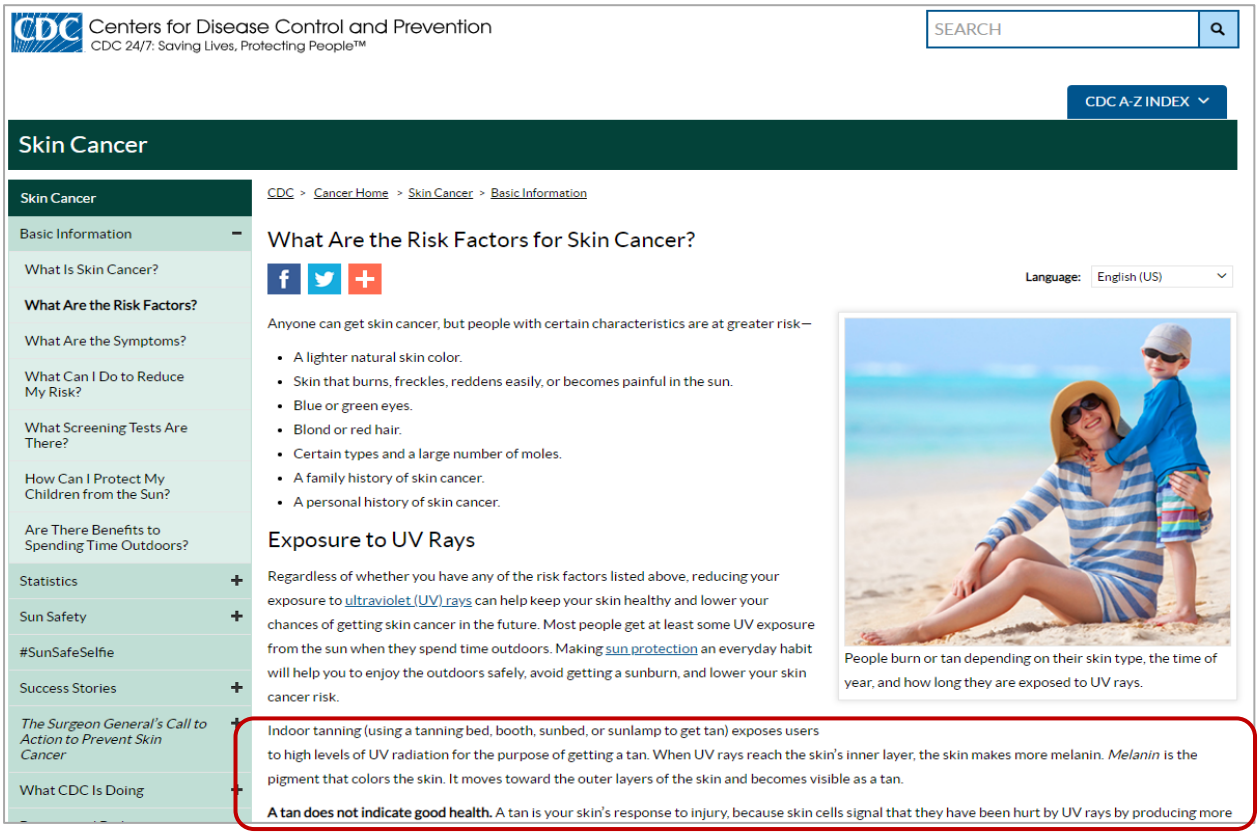
In 2005, the IARC Working Group on 'Exposure to Artificial UV Light and Skin Cancer' concluded there was convincing evidence to support a causal relationship between the use of UV-emitting (mostly UVA) indoor tanning facilities and risk of melanoma, particularly when the exposure occurs before the age of 35 years[2].

Volume 100D of the *Monographs* reviewed the evaluations for "UV radiation" and "Use of UV-emitting tanning devices" previously classified in Group 2A (*probably carcinogenic to humans*)[3]. Based on mechanistic data in UV-exposed experimental animals and humans, both exposures were raised to Group 1. UV-emitting tanning devices increase the risk of malignant melanoma of the skin and of the eye, with higher risks for people who first used tanning devices before age 30 or age 20, respectively. There is also a positive association with squamous cell skin cancer, especially when exposure occurs before age 20 years.

Soon after IARC published these conclusions, several organizations, including WHO, developed policies banning or limiting indoor tanning often directly citing the *Monographs* classification as the basis for the new recommendations. Brazil became the first country to ban indoor tanning for people of all ages, and Australia followed in 2015. Most recently France's national health security agency (ANSES) recommended a complete ban on commercial and personal indoor tanning devices. In view of the higher susceptibility of younger users, age restriction has been the more common type of action, especially during the past five years. In addition, research shows that laws with age restrictions are effective in reducing rates of indoor tanning among young women[5]. A total of 11 countries in Europe, each Canadian province, 17 States in the USA and New Zealand

have banned the use of indoor tanning for under age 18 years, and most other States in the USA have some restrictions for minors.

The Working Group Report and the *Monographs* evaluation of UV radiation and tanning devices are amongst the most successful examples of the impact of IARC's work in providing the basis for public health policy development for cancer prevention.



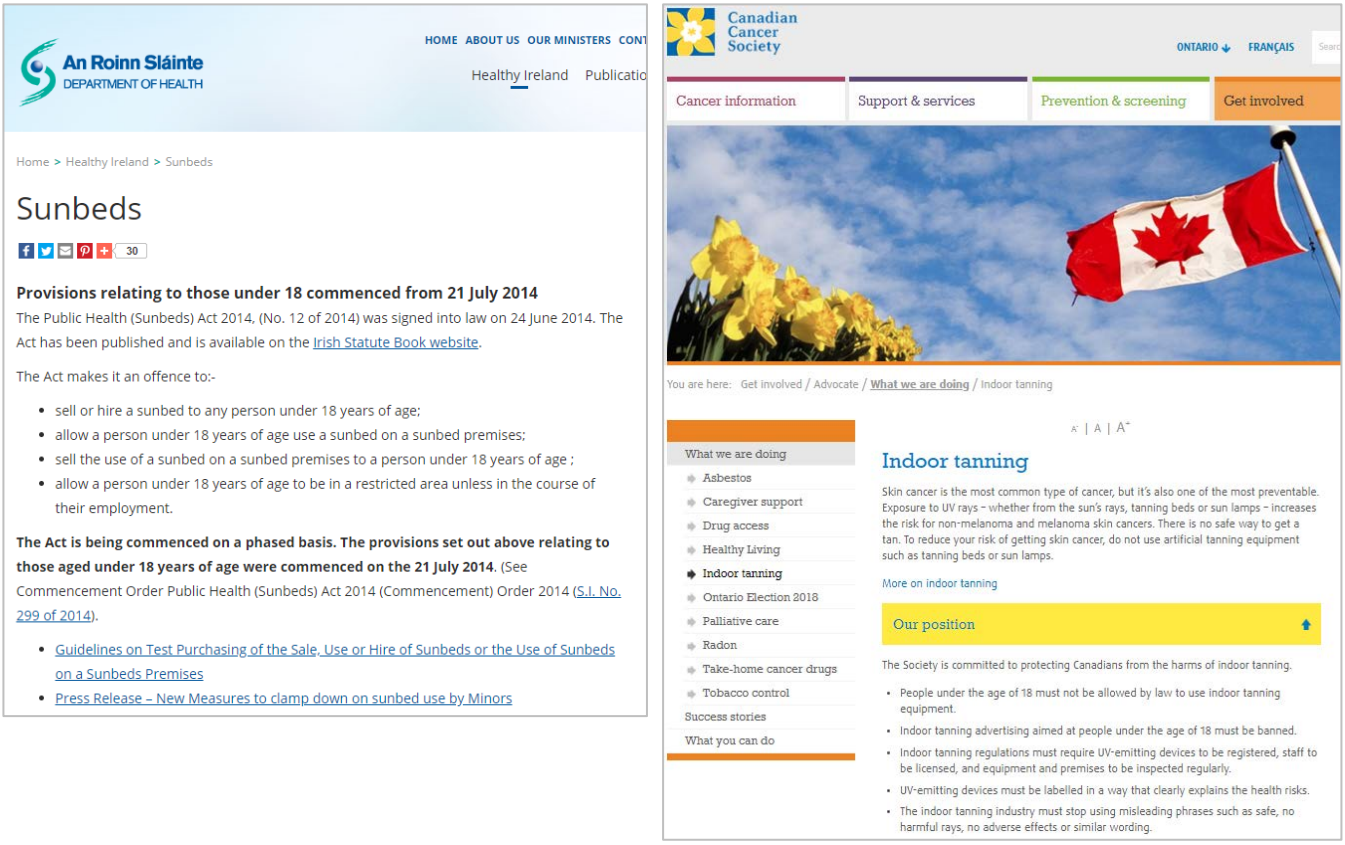


Figure – Examples of legislation and recommendations on the health effects of sunbeds (USA, European Union, Ireland and Canada)

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Case Study #6: IMPACT OF IARC MONOGRAPH VOL. 98 "SHIFT WORK THAT INCLUDES CIRCADIAN DISRUPTION" ON RESEARCH AND PRACTICE

MTS areas: These activities contribute to IARC MTS Project Tree objective 2.3 and 5.4

2.3 Provide expert evaluations of the available evidence-base to identify human carcinogens

5.4 Effectively communicate and disseminate the work of the Agency

IARC Sections/Groups involved: IARC Monographs (IMO)

Exposure to shift work involving circadian disruption is widespread. It has been estimated that 15-20% of workers in the USA and Europe and more than 30% of workers in Canada are employed outside the standard daytime work shift[1,2]. These percentages, which have been growing over time, vary by occupation and industry, with higher rates of shift workers in the manufacturing, medical, mining, hospitality, public safety, and transportation sectors.

In 2007, IARC Monograph 98[2,3] categorized shift work involving circadian disruption in Group 2A, based on limited evidence of carcinogenicity in humans and sufficient evidence in animals. A major limitation of human evidence was the crude and variable assessment of shift-work in the studies available at that time.

In 2009, a workshop was convened by IARC (with support from UK HSE and German DGUV) on methods to improve exposure assessment in epidemiologic studies of shift work. The resulting publication[4] was the most highly cited article in Occupational and Environmental Medicine contributing to the journal's new higher impact factor. The recommendations were supported by an interagency expert review group[5] and were implemented in many subsequent studies.

The impact of the shift work Monograph on research activity has been notable, stimulating many new cancer epidemiology studies of shift work and circadian disruption, including for cancer sites and in populations not previously studied, such as in LMIC. In the 10 years following the publication of the 2007 Lancet Oncology article, the number of PubMed citations on the topic was six times that in the previous 10 years (Fig.)[7], compared to a 1.5-fold increase in all Medline citations over the same time period[8].

The breadth of research citing the 2007 Lancet Oncology article encompasses a wide range of topics beyond epidemiologic studies of cancer in shift workers, including exploration of mechanisms in humans and animal models, development and application of biomarkers, and designing interventions to reduce the potentially harmful effects of shift work. More broadly, they encompass the evaluation of many other diseases and adverse conditions potentially caused by shift work involving circadian disruption as well as a renewed interest in fundamental aspects of cell cycle and chronodisruption in basic biological science.

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[7] Based on a PubMed search of the following terms: (shift work* OR shiftwork* OR night work* OR nightwork* OR night-time work* OR night shift* OR nightshift* OR working night* OR graveyard shift* OR (circadian AND disrupt*) OR Shift Work Schedule[MeSH]) AND (neoplasm* OR carcinogen* OR malignan* OR tumor OR tumors OR tumour OR tumours OR cancer OR cancers)

[8] https://www.nlm.nih.gov/bsd/stats/cit_added.html

This burgeoning of research on shift work since the Monograph 98 has resulted in the creation of a new MeSH term for Shift Work in 2018, which will greatly facilitate the identification of future research on the topic.

Another area of public health research inspired by the IARC evaluation was the inclusion of shift work in the development of estimates of the burden of occupational cancer in different populations[6]. Such estimates have found that shift work (if causal) explains at least half of the expected occupational cancer burden in women, from breast cancer alone.

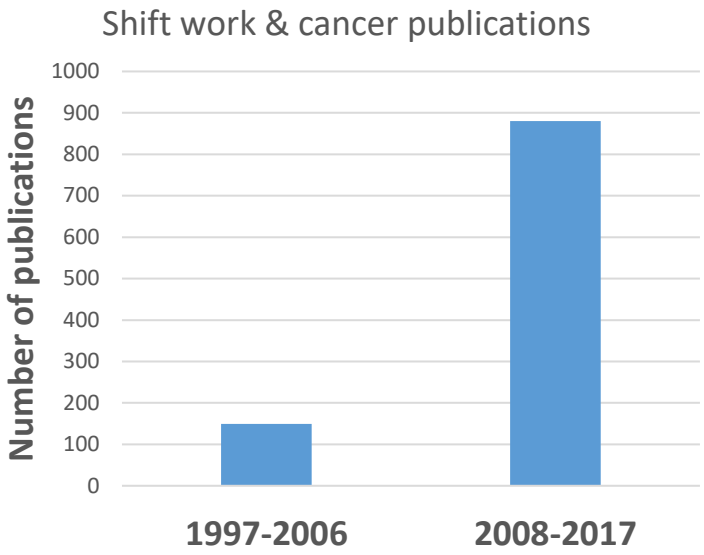

Figure – Number of publications referring to “shift work and cancer” in PubMed prior to and after the publication of the summary of Monograph 98 in the Lancet Oncology in 2007[3].

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Case Study #7: UN JOINT PROGRAM ON CERVICAL CANCER AND "ELIMINATION OF CERVICAL CANCER" INITIATIVE

MTS areas: These activities contribute to IARC MTS Project Tree objectives 1.1, 1.2, 2.1.1, 3.1, 3.2, 3.3, and 5.3, 5.4

- 1.1 Improve and expand reporting of descriptive cancer statistics
- 1.2 Support improved coverage and quality of cancer registration, particularly in low and middle-income countries
- 2.1.1 Advance understanding of the role of infectious agents
- 3.1 Enhance understanding of interventions for cancer prevention and control
- 3.2 Enhance the implementation of cancer prevention and control programmes
- 3.3 Provide expert evaluations of the available evidence-base in order to recommend prevention strategies
- 5.3 Create and maintain key strategic partnerships with national, regional and international organisations
- 5.4 Effectively communicate and disseminate the work of the Agency

IARC Sections/Groups involved: led by Prevention and Implementation (PRI) with contributions from Screening (SCR) Infections and Cancer Epidemiology (ICE), Infections and Cancer Biology (ICB), Cancer Surveillance (CSU) and IARC Handbooks of Cancer Prevention (IHB)

Cervical cancer, one of the leading female tumours responsible for 250 000 deaths a year mainly in low and middle-income countries is now one of the most preventable. Research over the last 30 years has discovered its cause, established its natural history and led to the development of extraordinary tools for primary and secondary prevention. The availability of safe and highly effective vaccines against the human papillomavirus (HPV) types responsible for the majority of cancers, in addition to new approaches to screening using HPV testing and new treatment approaches and algorithms, have dramatically changed the perspective for cervical cancer control. It is now feasibly to prevent 100% of new infections among adolescents vaccinated before initiation of sexual activity and to detect virtually all prevalent precancerous lesions and treat most of them with simplified methods.

IARC has played a pivotal role in the research leading to these extraordinary discoveries with contributions from Sections and Groups across the Agency. Some examples of IARC research activities contributing to the "Elimination of cervical cancer" initiative are listed in Figure 1.

The vast knowledge generated and the tools derived from the research have recently resulted in a call by the WHO Director-General to eliminate cervical cancer as a public health problem worldwide, in the context of a large initiative including all the United Nations Organizations related to health (WHO, IARC, UNICEF, UNAIDS, UNFPA, HRP, IAEA) called the UN Joint Program for cervical cancer control, that is coordinating implementation efforts for vaccination, screening and treatment of cervical cancer, defining the criteria for elimination of this serious public health problem. IARC continues its extensive research program on HPV and cervical cancer as an essential input for definition of policy and guidelines for cervical cancer control.

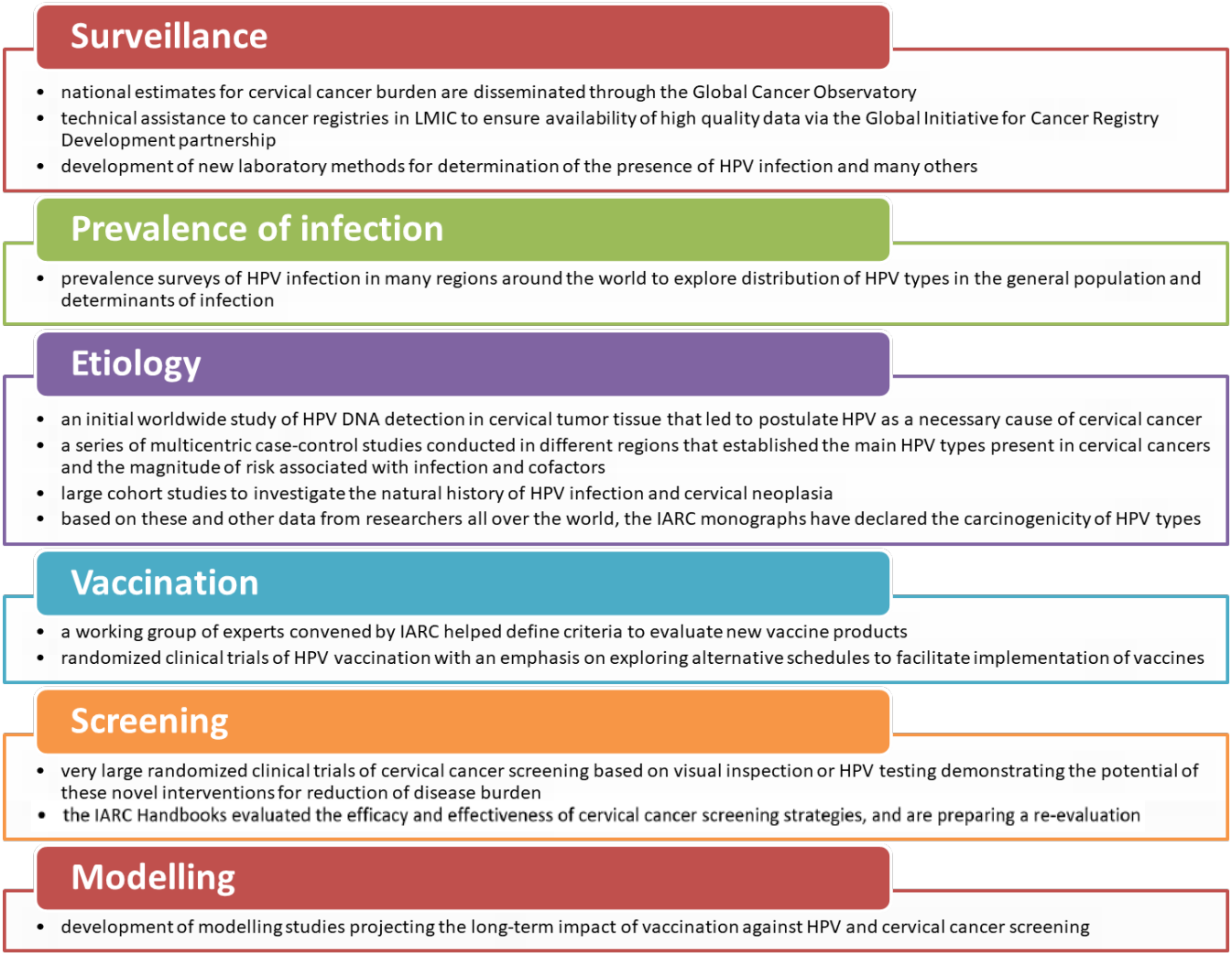


Figure 1 - Major contributions from IARC research activities in support of the “Elimination of cervical cancer” initiative

Case Study #8: THE SURVMARK-2 PROJECT: BENCHMARKING CANCER SURVIVAL IN HIGH INCOME COUNTRIES TO INFORM CLINICAL PRACTICE AND POLICY

MTS areas: These activities contribute to IARC MTS Project Tree objectives 1.1.1 and 3.1.3, and 5.4.1

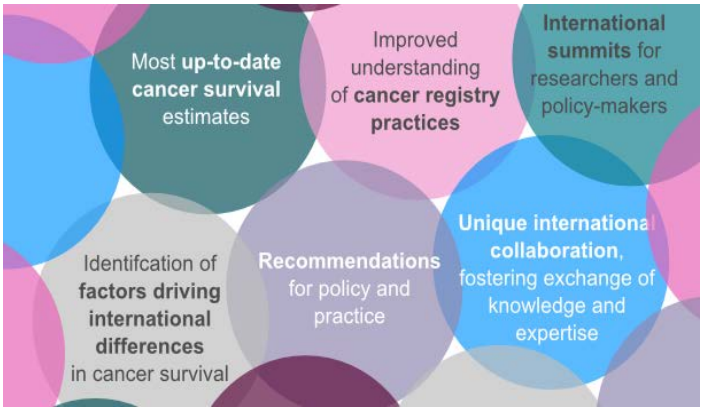
- 1.1.1 Expand the descriptive analyses of cancer incidence, mortality, prevalence and survival regionally and worldwide
- 3.1.3 Enhance understanding of the factors affecting cancer prognosis
- 5.4.1 Effectively communicate and disseminate the work of the Agency

IARC Sections/Groups involved: Cancer Surveillance Section (CSU)

Cancer survival provides a means to assess the effectiveness of early detection strategies and the quality of clinical care and management. Regular updates of a comprehensive set of survival indicators are needed, alongside the core set of complementary indicators of incidence and mortality.

SurvMark-2 is a multidisciplinary project coordinated at IARC involving clinicians, academics, data experts and policymakers that aims to develop a comprehensive and quality-assured set of country-specific indicators for benchmarking survival across countries and unpick the reasons for survival differences between countries as a basis for elimination of survival disparities in the near future.

At the end of the project, SurvMark-2 will provide the most recent cancer survival estimates using multiple indicators and presentational approaches, including synergetic analyses of incidence and mortality by country, period, sex, age and stage. Alongside the provision of high-quality survival estimates, the project includes an assessment of adherence to international standards of coding and classification (including stage), and the impact of variations in such practices on explaining survival differences, that will lead to the development of international guidelines to ensure robust data for international survival benchmarking.



IARC coordinates this project and it is well placed to foster the development of a more comprehensive set of indicators, an integrated assessment of factors linked to registration and coding including staging practices, and enhance communication with national partners. The section of Cancer Surveillance at IARC has long-standing expertise in coordinating international data collection supported by a secure data transfer and encrypted communication. It also has the skills, capacity and knowledge to harmonize datasets to fulfil international standards, whilst ensuring personal communication to data providers to guaranty the highest possible standard of data needed for action.

The SurvMark-2 project aims to significantly improve and expand the currently available data on cancer patients' survival internationally. Results of this project will include a diverse set of metrics with clear messages targeted to specific audiences that include patients, clinicians, academics, as well as governmental and non-governmental agencies.

Phase one of this multinational collaboration has been successful in driving clinical practice and policy changes in some countries. It is expected that SurvMark-2 will have an even greater impact by improving cancer patients' survival at national level and reducing inequalities between countries.

Case Study #9: MUTOGRAPHS OF CANCER: DISCOVERING THE CAUSES OF CANCER THROUGH MUTATIONAL SIGNATURES

MTS areas: These activities contribute to IARC MTS Project Tree objective 2.1.2 and 2.1.3

2.1.2 Advance understanding of the role of environmental, occupational and iatrogenic factors

2.1.3 Advance understanding of the role of dietary, metabolic and lifestyle factors

IARC Sections/Groups involved: led by Genetic Epidemiology (GEP) with contributions from Genetic Cancer Susceptibility (GCS) and WHO/IARC Classification of Tumours (WCT)

All cancers are caused by changes in the DNA of cells in the body that occur over the course of an individual's lifetime, so-called somatic mutations. Different patterns of somatic mutation, known as "mutational signatures", are generated by the different environmental, lifestyle and genetic factors that cause cancer. For example, tobacco smoke and ultraviolet radiation in sunlight both cause cancer by generating somatic mutations, but different mutational signatures are found in the lung and skin cancers they respectively cause. To date, more than 40 different mutational signatures have been reported. However, the environmental, lifestyle, genetic or other potential causes of many of these mutational signatures remain unknown.

MUTOGRAPHS is a 5-year project, initiated in May 2017, which involves conducting whole genome sequencing on 5000 individuals with cancer for 5 different cancer types across 5 continents to explore whether different mutational signatures in the DNA of cancers explain geographic differences in cancer incidence. The five cancer types are colorectal, renal, pancreatic, esophageal adenocarcinoma and esophageal squamous cancers which all have degrees of uncertainty in their aetiology. They were selected on the basis that they show major geographical and temporal differences in incidence and are suspected of being associated with exposures linked to ‘westernized lifestyles’ or with specific local exposures. We anticipate that this project will fill important knowledge gaps in our understanding of the aetiology of cancer, which is essential to design effective prevention measures.

MUTOGRAPHS is led by Prof Sir Mike Stratton (Wellcome Trust Sanger Institute, UK) and five co-Principal Investigators, including Dr Paul Brennan (IARC). IARC leads the recruitment of research participants from 30 hospitals in 20 countries. This is made possible thanks to IARC’s longstanding experience in coordinating large, multicentre recruitments and wide network of collaborations including many of the contributing centres.

MUTOGRAPHS will provide a catalogue of mutational signatures that can be quantified within each tumour tissue. The relative burden of each signature will be compared across countries with variable cancer incidence rates, hence informing on the relative impact of risk factors by countries. It also has the potential of discovering unsuspected causes of cancer through the identification of their fingerprints in the tumour itself.

MUTOGRAPHS represents an unprecedented approach to increase our understanding of the causes of cancer, that it is hoped will lead to new strategies for prevention, including through providing opportunities to improve early detection, refine high-risk groups for which screening strategies would be most beneficial, contribute to further therapeutic development and identify new modifiable risk factors.

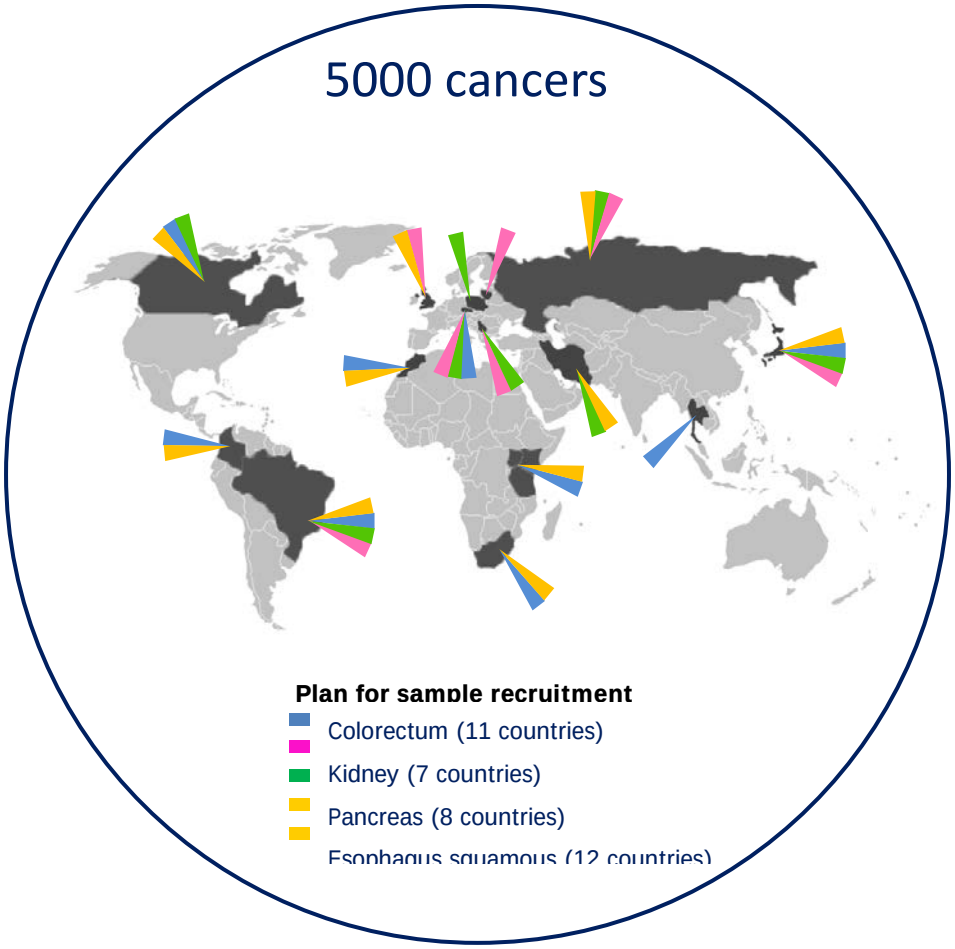


Figure – Map of MUTOGRAPHS sample recruitment

Case Study #10: ESTAMPA – MULTICENTRIC STUDY OF CERVICAL CANCER SCREENING AND TRIAGE WITH HPV TESTING

MTS areas: These activities contribute to IARC MTS Project Tree objectives 3.1.2, 3.2.1 and 4.1

- 3.1.2 Analyse the effectiveness of secondary cancer prevention strategies
- 3.2.1 Identify factors influencing the effective implementation of primary and secondary prevention programmes
- 4.1 Increase human resources for cancer research

IARC Sections/Groups involved: led by Prevention and Implementation (PRI) with contributions from Screening (SCR), Laboratory Services and Biobank (LSB) and WHO/IARC Classification of Tumours (WCT)

Cervical cancer remains a serious public health problem, particularly in LMICs where 90% of the nearly 250 000 global deaths from this cancer occur every year. Cytology-based screening, with few exceptions, has not been successful in reducing cervical cancer in LMICs. Detection of cervical HPV infection with high sensitivity and reproducibility is being used or considered to replace cervical cytology worldwide. However, HPV is a very common infection, most HPV infections are cleared by the immune system and only a few persist and progress to cancer. The current HPV tests identify almost all women with cervical lesions but at the expense of worrying many others who will not develop disease and of referring them for further examinations, inevitably overloading colposcopy clinics and potentially leading to overtreatment with the rare but non-negligible risk of complications. One of the main issues yet to resolve is how to select HPV positive women who are at risk of significant disease for further evaluation and treatment (triage).

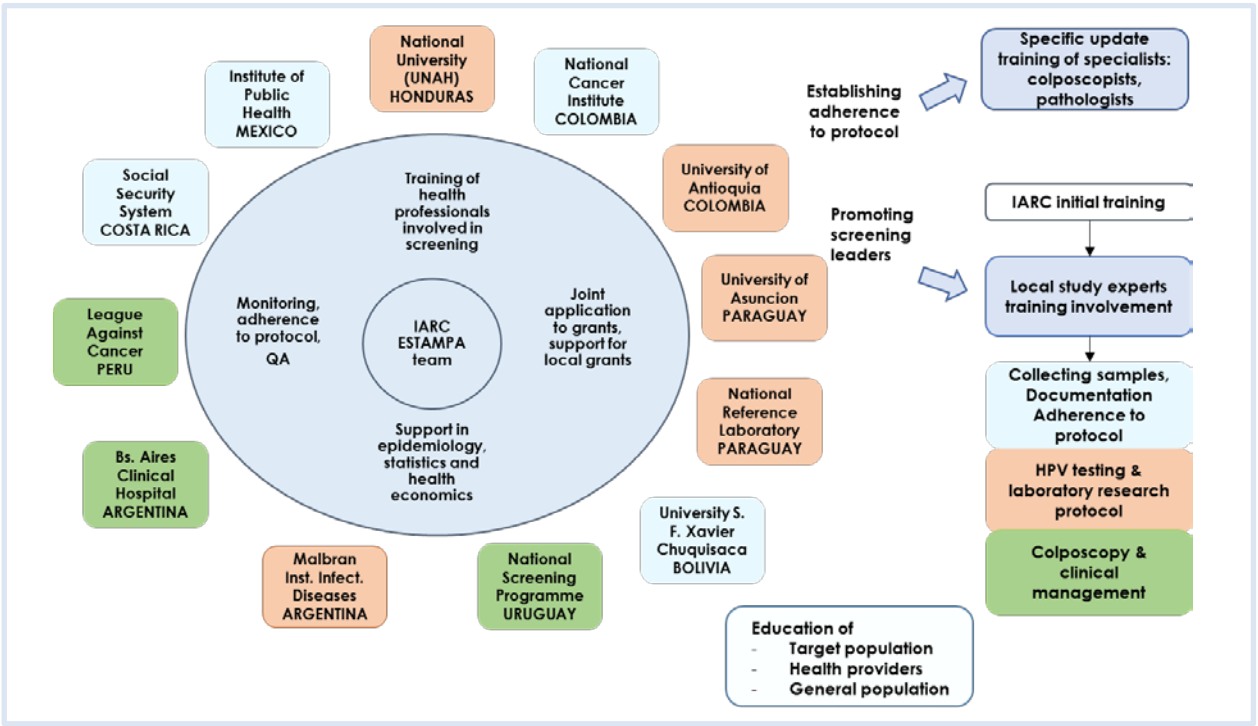
The multicentric study of cervical cancer screening and triage with HPV testing (ESTAMPA study) coordinated by IARC, aims to evaluate different visual-, cytological- and molecular-based screening techniques to triage HPV positive women, avoiding unnecessary anxiety and referrals. The study also evaluates approaches to overcome implementation challenges of HPV-based screening programs, including evaluation of strategies to reduce the negative psychosocial impact of testing positive for HPV using an already validated tool, the use of HPV self-sampling to increase screening participation, and strategies to establish affordable quality assurance.

The ESTAMPA study, aimed at recruiting 50,000 women in 12 centres located in nine countries of Latin America. Each centre is mostly funded by in-kind contributions from local health systems that allow the screening process in their facilities and the participation of a large number of health professionals engaged in sample collection (nurses, general doctors), HPV testing (laboratory technician, molecular biologists), diagnosis and treatment (pathologists, colposcopists) and overall coordination (research nurses, public health specialists). ESTAMPA investigators prepare grant applications with support from IARC to local or regional funding schemes, that financially support study activities and innovative research ideas.

Study personnel are trained in all aspects of the study, with special attention to ethics and safety of human participants, and specialists in colposcopy and pathology receive updates on diagnosis and clinical management of cervical pre-cancer. Study members from different centres form multidisciplinary teams that train new study centres and monitor activities all over the region.

ESTAMPA represents a particularly successful model of the impact of IARC's work in stimulating the development of local research infrastructure and capacity, through the creation and coordination of a research network, promoting good clinical practice, state-of-the-art knowledge on cervical cancer prevention, training of new cancer researchers in Latin America, and supporting the leveraging of local research funds by national partners. ESTAMPA will contribute to cervical cancer elimination by generating evidence on the implementation of HPV testing in primary screening and eventually leading to changes in practice, from fragmented opportunistic low-coverage cytology screening to affordable and sustainable HPV-based screening in the region.

Figure – ESTAMPA Study Network



Case Study #11: THE INTEGRATIVE ANALYSIS OF LUNG CANCER RISK AND AETIOLOGY (INTEGRAL) PROJECT

MTS areas: These activities contribute to IARC MTS Project Tree objectives 2.1.4 and 3.2.1

2.1.4 Advance understanding of the role of genetic factors in influencing risk, and their interaction with non-genetic factors

3.2.1 Identify factors influencing the effective implementation of primary and secondary prevention programmes

IARC Sections/Groups involved: Genetic Epidemiology (GEN)

Lung cancer causes one of every 5 cancer deaths, globally accounting for over 1.8 million deaths every year. Overall lung cancer survival rates are poor but vary strongly depending on clinical stage at diagnosis. Early detection through screening with low-dose computed tomography (CT) scans can reduce lung cancer mortality rates significantly. The two largest randomized trials of screening with low-dose CT scans, the US NLST trial and the European NELSON trial, have demonstrated important reductions in lung cancer mortality. However, CT-screening for lung cancer comes with significant financial and morbidity costs. Two open questions on low-dose CT screening include how to optimally identify those individuals who are most likely to benefit from CT-screening, and how to follow up individuals who present with indeterminate nodules on CT.

The INTEGRAL project is a comprehensive research programme, developed in collaboration between IARC, Baylor College in Houston, Texas, and Samuel Lunenfeld Research Institute of Mount Sinai Hospital, Toronto, aiming to improve the effectiveness of CT-screening by systematically developing and integrating information from a range of factors, including genetic host factors (Project 1, lead Baylor), circulating early detection biomarkers (Project 2, lead IARC), and radiomic nodule management (Project 3, lead Lunenfeld) (Figure 1).

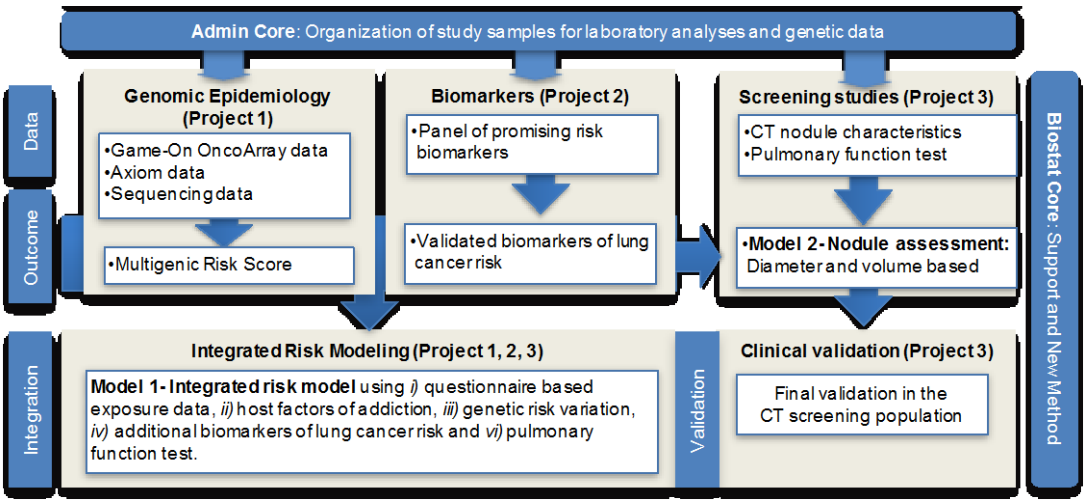


Figure – Conceptual Framework of the Integrative Analysis of Lung Cancer Risk and Etiology (INTEGRAL) research programme.

The INTEGRAL project leverages two world-leading resources for research on lung cancer that the IARC Genetics Section has been instrumental in developing, namely genome-wide genotyping data on 30 000 lung cancer cases and 55 000 controls (*Mckay et al., Nat Gen. 2018*), and pre-diagnostic biomarker measurements on 5 400 case-control pairs from 20 prospective population cohorts participating in the Lung Cancer Cohort Consortium (LC3) (*Fanidi et al. JNCI 2018*). The programme is supported with a research grant of $12 000 000 from the US NCI and started in April 2018.

Initial results from Project 2 on circulating early detection biomarkers, led by IARC, support the premise of the programme, showing that the integration of data from circulating tumour-related protein biomarkers into the current screening eligibility criteria increased the sensitivity of CT-screening from 43% to 63% in identifying future lung cancer cases (*Guida et al. JAMA Onc. 2018*).

The INTEGRAL programme is highly translational and has the potential to lead the development of early detection biomarkers for lung cancer, improve lung cancer risk models and screening eligibility criteria, as well as optimize work-up of individuals who present with positive nodules on CT. If successful, this will lead to more effective CT-screening programmes with reduced morbidity and ultimately preventing more lung cancer deaths.

Case Study #12: THE EXPOSOMICS PROJECT

MTS areas: These activities contribute to IARC MTS Project Tree objectives 2.1, 2.2, 4.2 and 4.3

- 2.1 Identify the risk factors for human cancer through the conduct of epidemiological studies
- 2.2 Elucidate mechanisms of carcinogenesis through the conduct of laboratory studies
- 4.2 Develop new methodologies for cancer research
- 4.3 Provide the resources and infrastructure to support and enhance research

IARC Sections/Groups involved: led by Epigenetics (EGE) and Biomarkers (BMA) with contributions from Nutrition and Epidemiology Group (NEP), Nutritional Methodology and Biostatistics, (NMB) and Communications (COM)

The concept of the 'exposome' was proposed to describe all exposures to which an individual is subjected from conception to death[1]. Unravelling the role of environmental factors that may contribute to cancer risk in large prospective studies requires accurate exposure data. However, measurement of the many environmental exposures that an individual is subjected to, even over a limited period of time, constitutes a considerable challenge.

The EXPOsOMICS project involved partners from 12 leading institutions (11 European and 1 in the USA) with expertise in exposure assessment, omics analyses, biostatistics and epidemiology. The project aimed at developing new approaches based on omic technologies to assess environmental exposures, focusing primarily on air pollution and water contaminants, by linking exposure data to biochemical and molecular changes in the body. A holistic approach integrating environmental, personal monitoring and biochemical measurement was applied to short-term experimental studies and long-term epidemiological studies on adults, children and new-borns to refine exposure assessment.

IARC has developed unique capacity to apply metabolomics and epigenomics analyses in large cohort studies. It was responsible for all metabolomic analyses in the EXPOsOMICS project and successfully established and applied different methodologies for high-throughput and genome-wide epigenetic analysis that have proven their importance in EXPOsOMICS as well as in several other major multidisciplinary projects. Markers of environmental exposures were analyzed jointly with downstream metabolic effects in 3 intervention studies (Oxford Street, TAPAS and PISCINA studies) and 6 observational studies. The effect of maternal air pollution exposure on birth weight was studied in four European birth cohorts (INMA, Piccolipiu, Environage, RHEA).

IARC's expertise in generating and analyzing metabolomic and epigenomic data enabled a switch from candidate-gene approaches to unbiased characterization of hundreds of thousands of metabolic and epigenetic features in a large series of samples in a single assay. Successful completion of metabolome and methylome profiling of 2 500 samples from different EXPOsOMICS cohorts across the life course clearly demonstrated the robustness of IARC's wet lab and bioinformatics pipelines and the capacity to develop critical laboratory tools applicable to population-based cohorts and molecular epidemiology.

The analysis of epigenomic and cross-omic data in EXPOsOMICS successfully established the link between epigenetic changes and air pollution exposures (particulate matter). In addition, the epigenome data generated within EXPOsOMICS projects were instrumental in promoting new collaborations among major international consortia that encompass early life exposure and child cancer, including the International Childhood Cancer Cohort Consortium (I4C), the Pregnancy and Childhood Epigenetics (PACE) consortium, the Environment and Child Health International Birth Cohort Group consortium.

IARC has made a key contribution within the EXPOsOMICS project to the characterization of key components of the exposome thus contributing to a step-change in addressing the risk factors for cancer. Ongoing analyses of metabolic, epigenomic and cross-omics data generated by IARC within the EXPOsOMICS project is expected to identify new biomarkers of exposure and cancer risk and contribute to the development of novel approaches for the assessment of exposure to high priority environmental carcinogens.

References

1. Wild CP (2005) Complementing the genome with an "exposome": the outstanding challenge of environmental exposure measurement in molecular epidemiology. Cancer Epidemiol. Bio. Prev. 14: 1847-1850

Case Study #13: TRANSLATIONAL STUDIES OF HEAD AND NECK CANCER IN SOUTH AMERICA AND EUROPE

MTS areas: These activities contribute to IARC MTS Project Tree objectives 2.1 and 3.1

2.1 Identify the risk factors for human cancer through the conduct of epidemiological studies

3.1 Enhance understanding of interventions for cancer prevention and control

IARC Sections/Groups involved: Genetic Epidemiology (GEP) and Genetic Cancer Susceptibility (GCS)

Head and neck cancers (HNC) are mostly comprised of oral cavity, oropharynx, hypopharynx, and larynx tumours. When taken together, HNC represent the 6th most common cancer globally, with 513 124 (6.9%) of all new cancers annually, and is the 5th most common malignancy among men. HNC generally have a very poor prognosis when diagnosed at later stages.

HEADSpAcE is a new project that builds upon over 20 years of collaboration between IARC, investigators in Europe and South America regarding the aetiology of HNC. The aims of HEADSpAcE are to understand reasons for delay of diagnosis of HNC in order to reduce the proportion of these cancers that are diagnosed at a very late stage, and also provide evidence to improve care and reduce treatment-related morbidity by identifying other strong predictors of prognosis.

IARC will be the principal coordinator of this project involving 15 partners. The project is possible thanks to the experience of IARC in previous HNC studies including the recruitment of large series of cases in South America (INTERCHANGE) and in Europe (ARCAGE), and representing an extensive biorepository maintained at IARC. HEADSpAcE will be responsible for the recruitment of an additional 1100 new cases in 11 centres (including the development of the protocol, the questionnaire, the SOP for the sample retrieval, preparation and shipment), building on the 3000 cases from previous IARC led studies.

HEADSpAcE will contribute to understanding the causes of cancer through its primary objectives:

1. Assess the socio-economic and logistical reasons behind delay to diagnosis
2. Determine the most accurate way to assess HPV positive oropharynx cancer in the clinical setting
3. Identify the extent of HPV positive OPC in Europe and South America, and assess lifestyle and genetic predictors of HPV infection
4. Conduct comprehensive genomic evaluation of 800 HNC from South America and Europe.
5. Perform an analysis of germline variation to identify susceptibility loci for HNC outcome
6. Identify whether liquid biopsies can be informative for HNC clinical care
7. Identify guidelines for implementation into clinical care

HEADSpAcE will provide evidence of the primary reasons behind early detection of HNC, diagnosis of HPV+ HNC and prognosis of HNC as well as treatment guidelines and this will have an immediate impact on HNC care.

Case Study #14: AGRICOH: A CONSORTIUM OF AGRICULTURAL COHORT STUDIES

MTS areas: These activities contribute to IARC MTS Project Tree objectives 2.1.2

2.1.2 Advance understanding of the role of environmental, occupational and iatrogenic factors

IARC Sections/Groups involved: Environment and Radiation Section (ENV)

The Agricultural Cohorts Consortium (AGRICOH) was established in 2010 under an initiative led by IARC and the US National Cancer Institute (NCI). It presently includes 29 agricultural cohort studies from 12 countries addressing a wide range of occupational, environmental, lifestyle and other exposures as determinants of health and disease in farming populations. A larger sample size is crucial to investigate potential risks with greater precision when researching rare diseases such as cancer, particularly at the sub-type level, in association with infrequently occurring exposures. The aim of AGRICOH is to foster and enable data pooling from various cohorts internationally to achieve greater statistical power when investigating exposure-outcome associations (https://agricoh.iarc.fr).

In the first completed project in AGRICOH, IARC studied with their international partners the relationship between use of 14 pesticide chemical groups including 33 active ingredients and the incidence of Non-Hodgkin lymphoma (NHL) overall, and by sub-type, in over 300 000 farmers of 3 cohorts from France, Norway and the US. The study was funded by the French ONEMA and by IARC with additional contributions from the US NCI. NHL, encompassing sub-types with heterogeneous aetiology, is among the very few malignancies for which farmers have shown excess incidence and mortality in different parts of the world. Published individual studies exploring the association between specific pesticides and NHL, rarely covering sub-types, and often statistically underpowered, have generally shown risk estimates of modest magnitude, high statistical uncertainty, and inconsistent results, with very few exceptions, and thus the role of pesticides as cancer risk factors in farmers remains elusive.

IARC, as coordinator of the AGRICOH consortium, was the leader for this international pooling project. Analysis of the pooled data has generated combined risk estimates of NHL in association with specific pesticides in occupationally exposed individuals enrolled in cohort studies and identified significant associations of 2 active ingredients in pesticides with 2 NHL sub-types that will contribute to the present debate on the carcinogenicity of some pesticides.

Studies of the association between pesticide use in farmers and NHL have relevance to the general population, frequently exposed to some of the same pesticides domestically and environmentally. This project has developed pesticides crop-exposure matrices for Norway and exposure-assessment analyses codes easily adaptable to study the association of pesticides with other cancers in this and in additional cohorts.

Figure – Example of exposure to agricultural pesticides

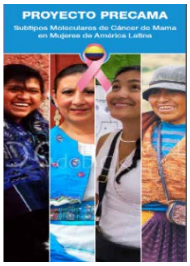
Figure – AGRICOH study group meeting, December 2018, Lyon.

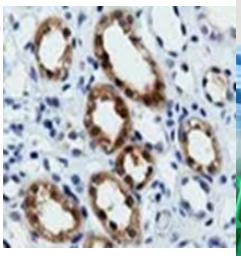
Case Study #15: PREMENOPAUSAL BREAST CANCER IN LATIN AMERICAN WOMEN – PRECAMA

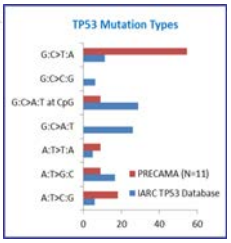
MTS areas: These activities contribute to IARC MTS Project Tree objectives 2.1.3, 2.1.4 and 4.1

- 2.1.3 Advance understanding of the role of dietary, metabolic and lifestyle factors
- 2.1.4 Advance understanding of the role of genetic factors in influencing risk, and their interaction with non-genetic factors
- 4.1 Increase human resources for cancer research

IARC Sections/Groups involved: led by the Nutrition and Metabolism Section (NMB) with contributions from the Molecular Mechanisms and Biomarkers (MNB) and Education and Training (ETR) Groups





Over the past twenty years the incidence and mortality of breast cancer in Latin America has increased rapidly to become the leading cause of cancer mortality among women in the region. Little is known about the causes and specific risk factors for premenopausal breast cancer, though hormonal exposures, diet, obesity and physical activity are hypothesized to play an important role. Risk factors for breast cancer in premenopausal women may differ according to hormonal receptor expression and molecular pathological characteristics and there is very little data on the distribution of these breast cancer subtypes in women in Latin America and in other developing regions.

The PRECAMA project is a large, multicentre population-based case-control study in Latin America established by IARC in collaboration with local partners to study the aetiology of breast cancer and determinants of survival in young women. The PRECAMA study will advance the prevention and management of breast cancer in Latin America through a better understanding of the molecular, pathological, and risk factor patterns, with a special focus on the role of dietary, metabolic and lifestyle factors. The study involves recruitment of breast cancer cases and controls in Mexico, Costa Rica, Chile, Colombia, and Brazil, for whom information on lifestyle, diet, and environmental factors, as well as blood, urine and tumour samples are being collected.

The PRECAMA study is in the recruitment phase but already includes more than 500 cases and 500 controls. With a target sample size of 1,500 cases and 1,500 controls, this project will be the largest ongoing effort to characterize the relationship between different BC subtypes and risk factors in young, premenopausal women in the region.

PRECAMA will be instrumental to provide evidence for addressing still-unanswered questions regarding breast cancer aetiology in young Latin American women, including: 1) what are the molecular phenotypes of breast cancer in this group and do they differ from those in other populations; 2) which reproductive (age at menarche, breastfeeding) and lifestyle (obesity, physical activity, diet) factors are specifically associated with major breast cancer subtypes; 3) what is the role of ancestry and genetic variants involved in metabolic disorders; 4) which factors may play a role in breast cancer progression, recurrence, and survival in Latin American women?

An improved understanding of the above molecular characteristics will allow clinicians to better understand the context in which breast cancer is detected and select, among the existing treatment options, those that are the most effective for Latin American patients. This will immediately improve diagnosis and treatment. Knowledge of determinants of breast cancer incidence and progression will provide a foundation for prevention strategies and improved survival.

Importantly, this project has enabled the creation of a strong collaborative network, which is strongly supporting the development of research infrastructure and capacity building through research, including specific pathology training. Overall, aside from PRECAMA itself, the project is strengthening breast cancer research in Latin America.

Case Study #16: ESOPHAGEAL SQUAMOUS CELL CANCER AFRICAN PREVENTION RESEARCH – ESCCAPE

MTS areas: These activities contribute to IARC MTS Project Tree objectives 2.1.2, 2.1.3 and 4.1.1

- 2.1.2 Advance understanding of the role of environmental, occupational and iatrogenic factors
- 2.1.3 Advance understanding of the role of dietary, metabolic and lifestyle factors
- 4.1.1 Award fellowships and provide training through participation in collaborative research projects

IARC Sections/Groups involved: Environment and Radiation Section (ENV)

Esophageal cancer is extremely rare in much of West Africa, yet in an easterly lying African corridor including Ethiopia, Kenya, Tanzania and Malawi, this is the third most common cancer and a leading cause of cancer death. Although the extraordinarily high incidence of this cancer was documented over 50 years ago, little aetiologic research has been conducted in the continent outside of South Africa. Thus in 2013, facilitated by IARC seed funding, the Agency initiated pilot studies of risk factors for esophageal squamous cell carcinoma, the most common histological subtype, in these East African settings, which subsequently succeeded in attracting external funding from the US NIH.

The resulting multi-country East African case-control study, ESCCAPE, has recruited 2000 cases and controls to date and is already providing robust evidence to inform much needed primary prevention of esophageal cancer in East Africa.

IARC's leadership of this East African initiative has been successful due to several factors:

- First, the combination of leadership, professional networks and cultural knowledge at the local level, together with IARC's epidemiological and technical expertise, forms multidisciplinary teams who can smoothly conduct sound studies, designed to address risks posed by locally-relevant exposures and exposure circumstances.
- Second, ESCCAPE is part of a wider portfolio of IARC fieldwork now ongoing in 9 sub-Saharan African countries, through which valuable experience has been obtained on study coordination to reduce risk of research investment in such settings with more fragile health systems.
- Third, IARC's work is highly respected and as WHO's cancer research agency, entry points and relationships are easily developed to bring together local institutions.
- Further, the nature of the collaboration, which builds scientific knowledge through respect of study participants, capacity building, infrastructure strengthening and knowledge exchange, increases motivation for all team members and has developed mutually respectful long-term relationships.

IARC investment in ESCCAPE is now reaping important findings for this preventable cancer. For alcohol, for the first time the study was able to perform a detailed assessment of the contribution of local brews and spirits (chang'aa "kill me quick" in kiswahili, gongo or kachasu). Thermal injury also increases risk, and IARC studies in Tanzania have documented the world's highest measured

tea drinking temperatures to date. Finally, ESCCAPE has newly discovered strong cancer risk factors in this setting – related to poor oral health[9] - that will likely lead to important cancer prevention in East Africa in coming decades.

ESCCAPE has benefitted from the IARC summer school (7 attendees), two IARC-UICC development fellowships, biobanking support and pathology training, as well as molecular studies led by other Groups at IARC. One PhD has been completed, one started and one is being planned within the project.

With cancer epidemiology in its infancy in many parts of the world, ESCCAPE illustrates that substantial carcinogens are likely still yet to be discovered in many LMICs less-prepared to treat their increasing cancer burden.

Figure – Traditional alcohol brewed in Malawi (kachasu)

Figure – ESCCAPE annual meeting at the Kilimanjaro Clinical Research Institute, February 2017, which brought together clinicians and researchers from across the Kilimanjaro Region of Tanzania, as well as IARC ENV and GEP Sections.

[9] http://www.who.int/oral_health/en/

Case Study #17: IMPROVING NATIONAL CAPACITY TO PRODUCE CANCER SURVIVAL ESTIMATES IN LOW AND MIDDLE INCOME COUNTRIES – THE SURVCAN-3 PROJECT

MTS areas: These activities contribute to IARC MTS Project Tree objectives 1.1, 1.2, 1.1.1, 3.1.3 and 5.4.1

1.1 Improve and expand reporting of descriptive cancer statistics
1.2 Support improved coverage and quality of cancer registration, particularly in LMICs
1.1.1 Expand the descriptive analyses of cancer incidence, mortality, prevalence and survival regionally and worldwide
3.1.3 Enhance understanding of the factors affecting cancer prognosis
5.4.1 Effectively communicate and disseminate the work of the Agency

IARC Sections/Groups involved: Cancer Surveillance Section (CSU)

Cancer survival is increasingly being recognized as a key measure of overall effectiveness of the health system. Population-based survival studies that have systematically analysed the survival outcomes of cancer patients are readily available in Europe, North America and other more-developed regions, however there are generally few data available in developing countries. Previously, IARC published two landmark publications (SURVCAN-1 in 1999 and SURVCAN-2 in 2011) that assessed and benchmarked cancer survival as an indicator of population health impact in developing countries. The first volume examined data from 10 population-based cancer registries in five countries, while the second expanded coverage to 27 population-based cancer registries in 14 countries in Asia, Central and South America and Africa. SURVCAN-3 enlarges this to 90 cancer registries in Asia, Central and Latin America and Africa.

The principles of the project are to ensure there is local capacity to develop reliable and comparable survival statistics in LMIC. The data submitted by each registry are assessed by an editorial team that, as with Cancer Incidence in Five Continents, transmits specific issues and recommendations to improve data quality. Throughout the project, registries are supported to attain the necessary data required to participate through technical and financial support where required, in order to increase within country capacities to collect high-quality data and produce survival indicators.

IARC coordinates the data collection, harmonisation and analysis. It also provides face-to-face workshop and webinars on various aspects from data collection, data quality assurance through to data analysis, interpretation, and their translation to clinical decision-making. IARC is well placed to coordinate this project due to the extensive collaborations with registries worldwide, via the International Association of Cancer Registries (IACR) and the Global Initiative for Cancer Registry Development (GICR).

The project improves the current information on cancer patient's survival in LMIC and also increases the validity of the survival estimates originating from countries in transition. In addition to this, local registries benefit from improving the quality of the data, and the necessary skills to analyse and interpret local survival estimates for local planning. Results of the SURVCAN-3 project will provide valuable data to national policy makers in lower-resource settings, forming the baseline for assessing progress in reducing premature mortality from cancers through adequate and determined investments in improving awareness, health services infrastructure and accessibility for cancer care.

Figure – Training course on methodology for population-based survival studies, June 2017, Lyon.

Case Study #18: INVESTIGATING THE CAUSES OF CANCER IN A LARGE-SCALE EUROPEAN CONSORTIUM: THE EPIC COHORT

MTS areas: These activities contribute to IARC MTS Project Tree objectives 2.1.3, 2.1.4, 2.2.2 and 4.1.1

- 2.1.3 Advance understanding of the role of dietary, metabolic and lifestyle factors
- 2.1.4 Advance understanding of the role of genetic factors in influencing risk, and their interaction with non-genetic factors
- 2.2.2 Apply biomarkers to studies of cancer causes and molecular genetic classification of tumours
- 4.1.1 Award fellowships and provide training through participation in collaborative research projects

IARC Sections/Groups involved: Section of Nutritional and Metabolism (NME) and Section of Genetics (GEN) with the Laboratory Services and Biobank Group (LSB)

The European Prospective Investigation into Cancer and Nutrition (EPIC) is a longitudinal cohort that was established between 1992-1999 enrolling more than 521 000 study participants aged 35-70 from 23 centres in Denmark, France, Germany, Greece, Italy, Netherlands, Norway, Spain, Sweden and the United Kingdom. The EPIC cohort was established as an IARC initiative with close collaboration with the regional centres, and was funded by the European Commission with support from the local participating states. The cohort remains one of the largest longitudinal cohort studies in the world.

Figure – EPIC study centres

EPIC was established primarily to investigate the role of nutrition in cancer development and the multi-country design was intended to capture variation in diet and lifestyle habits across Western European countries. While a focus on the role of nutrition and metabolic factors in cancer development remained prominent, the cohort now also serves as in important resource for research on all aspects of cancer aetiology and survival as well as the study of other chronic diseases. EPIC is jointly coordinated by IARC and Imperial College London and is governed by a steering committee comprising representatives from each EPIC centre.

Detailed information on diet, lifestyle characteristics, anthropometric measurements, and reproductive and medical history was collected at recruitment. Biological samples including plasma, serum, leukocytes, and erythrocytes were also collected at baseline from 387 889 individuals and are stored at IARC and mirrored at EPIC collaborating centres. IARC maintains the centralized EPIC database and serves as the hub for data centralization and dissemination to investigators for analyses. Follow-up of study participants is coordinated by the individual EPIC

centres through cancer registry linkage or active follow-up. IARC is now engaged in coordinating centralization of diet and lifestyle data collected during follow-up.

The long-term follow-up coupled with the large sample size of the cohort means a substantial number of EPIC participants have now developed cancer. Since recruitment, approximately 67 000 members of the cohort have been diagnosed with cancer and more than 70 000 have died. The large number of incident cancers means that it is now possible to perform detailed analyses on cancer subtypes (e.g. molecular subtypes, anatomic location) for more common cancers such as breast and colorectum, while for rarer tumours it is now possible to investigate risk factors with greater precision.

The impact of the EPIC study has been remarkable. As a consortium EPIC has produced more than 1200 scientific articles with notable publications on the role of diet, alcohol, obesity and metabolic factors with cancer and other health outcomes, as well as viruses and genetic factors. For example, EPIC was one of the first studies providing robust evidence on the link between adiposity, cancer and mortality demonstrating that obese men had a 2.7-fold higher risk of death from colorectal cancer over the follow-up period compared to those of normal weight, while among women, obesity conferred a 1.6-fold higher risk of breast cancer-related death compared to lean individuals. The EPIC study has also provided convincing evidence for a beneficial effect of adherence to the Mediterranean diet on survival in older age and lower risk of cancer. Many of these studies have provided the core evidence for assessments of cancer risk factors, such as the IARC Monograph on red and processed meat (Vol. 114) or the IARC Handbook on body fatness (Vol. 16), informing the development of guidance and policy in these and many other areas.

EPIC has also made substantial contributions to international consortia, for example for genome-wide association studies. Important sub-studies within EPIC include EPIC-Interact and EPIC-Heart – case-cohort studies designed to investigate the aetiology of type 2 diabetes and cardiovascular disease, respectively; EPIC-PANACEA – a study of the causes of weight gain and obesity, and NeuroEPIC4PD which has a focus on Parkinson's disease. The cohort now serves as an important and growing resource for future studies employing new molecular technologies (e.g. metabolomics, proteomics) to identify the causes of cancer and other chronic diseases as well as identify early markers of cancer.

Case Study #19: INTERNATIONAL CHILDHOOD CANCER COHORT CONSORTIUM – I4C

MTS areas: These activities contribute to IARC MTS Project Tree objectives 2.1.4, 2.2, 4.2, and 4.3

- 2.1.4 Advance understanding of the role of genetic factors in influencing risk, and their interaction with non-genetic factors
- 2.2 Elucidate mechanisms of carcinogenesis through the conduct of laboratory studies
- 4.2 Develop new methodologies for cancer research
- 4.3 Provide the resources and infrastructure to support and enhance research

IARC Sections/Groups involved: led by Epigenetics (EGE) with contributions from Genetic Cancer Susceptibility (GCS), Infections and Cancer Biology (ICB), Biomarkers (BMA) and Laboratory Services and Biobank (LSB)

Several well-designed individual case-control studies have contributed to our current knowledge on risk factors of childhood cancer. However, case-control studies that rely on subject participation may be limited by selection bias, recall bias for certain exposures, lack of specificity of exposure, and, in the case of relatively rare cancers such as childhood cancers small number of cases, which will affect risk estimates and interpretation.

The International Childhood Cancer Cohort Consortium (I4C) encompasses 7 cohorts with more than 388 120 mother/child pairs, including 675 children diagnosed with cancer to date. The cohort design offers unique opportunities to better understand temporality and specificity of agents leading to childhood cancer, especially through the analysis of pre-diagnostic measurements or biological samples to assess exposure.

The Agency has led the identification and successful acquisition of biospecimens from the I4C cohorts, becoming the I4C Biospecimen Coordinating Centre (IBCC). The two largest childhood cancer cohorts worldwide have already provided samples to I4C through IARC, which has successfully coordinated elaborate scientific, administrative and legal agreements with the relevant cohorts.

Although I4C initially started with a purely epidemiological design IARC has played a central role in introducing molecular epidemiology approaches into the consortium. This was catalyzed by the development of methods and expertise at the Agency for extracting high quality DNA from archived biospecimens that have limited DNA content, such as neonatal blood spots, while also demonstrating the applicability of high-throughput omics analysis based on these precious samples, which offer a valuable ‘prospective’ molecular profile of early-life factors before cancer diagnosis.

Moreover, IARC has developed a unique capacity to apply high-throughput genome-wide epigenomics analyses in large cohort studies based on well-designed interdisciplinary pipelines interfacing between epidemiology and molecular biology. Accordingly, the Agency leads the coordination of all epigenomic analyses of the I4C and is involved in organizing all the annual meetings of this consortium.

The introduction of molecular epidemiology approaches in I4C has had important implications in the identification of novel risk factors, biomarkers, mechanisms of action as well as exposure assessment (such as epigenetic signatures of tobacco smoking, air pollution, birthweight, etc...). Such implications have helped IARC create synergies between the I4C and other childhood cancer consortia, including the Childhood Leukaemia International Consortium (CLIC), the Pregnancy and Childhood Epigenetics (PACE) consortium, the Environment and Child Health International Birth Cohort Group consortium and EXPOsOMICS. These consortia, based on large population studies, have helped feed data into the I4C on molecular signatures of early-life factors, which can be linked to childhood cancer outcomes.

Successful completion of profiling of epigenomes of thousands of samples from I4C, PACE and EXPOsOMICS cohorts is a clear demonstration of the robustness of IARC's wet lab and bioinformatics pipelines and its capacity to develop critical laboratory tools applicable to population-based cohorts and molecular epidemiology. In addition, the Agency has invested in establishing cross-omic analysis platforms that have helped better characterize associations between exposure and health outcomes, including causal inferences.

Ongoing analyses of epigenomic and cross-omics data generated by IARC within the I4C and related consortia is expected to identify new biomarkers of early-life exposures and childhood cancer risk and contribute to the development of novel approaches for the assessment of exposure to high priority environmental carcinogens or lifestyle factors.

Case Study #20: COLLABORATION WITH THE INTERNATIONAL ASSOCIATION OF CANCER REGISTRIES – IACR

MTS areas: These activities contribute to IARC MTS Project Tree objectives 1.2 and 1.3

1.2 Support improved coverage and quality of cancer registration, particularly in low and middle-income countries (LMIC)

1.3 Improve WHO tumour classification to inform cancer registration, research and treatment

IARC Sections/Groups involved: led by the Cancer Surveillance Section (CSU) with contributions from the Education and Training Group (ETR)

IARC's long-standing collaborative relationships with cancer registries worldwide — members of the International Association of Cancer Registries (IACR) — remain vital to improving the quality and use of cancer registry data at national, regional, and global levels. The partnership in the development of IACR registry standards to ensure international comparability of data is equally important; each volume of Cancer Incidence in Five Continents is a joint IACR-IARC collaboration.

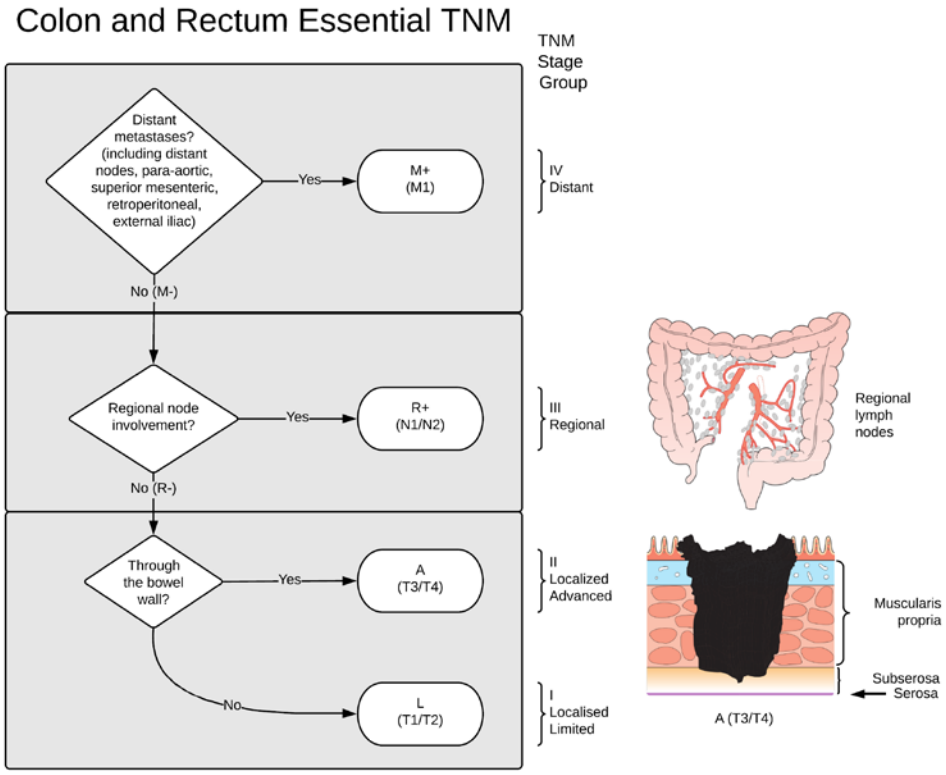
One key emphasis of the cooperation has been the development of a simplified staging system, *Essential TNM*, to be used by cancer registries in the absence of full data - the approach is to identify the most advanced disease form, summarizing the extent of disease in the order of distant metastasis (M), regional lymph node involvement (N) and tumour size/extension (T). Flowcharts and rules have been developed for coding these elements and combining them into stage groups (I-IV) that correspond to those obtained by full TNM staging; their utility has been assessed in a validation exercise involving several cancer registries in different settings, and a paper is published in Lancet Oncology describing the Essential TNM principles[1].

IARC and IACR have also been involved in the updates to the International Classification of Diseases for Oncology (ICD-O) ICD-O-3.1 and ICD-O-3.1, based on the revised editions of the WHO Classification of Tumours. With the upcoming changes in histopathology classification of tumours, the recently published ICD-11, a new structure and reorganization is required for ICD-O-4. An IARC/IACR Working Group has been established to discuss with WHO and IARC/WCT these aspects and ensure alignment with registry practices.

While the basic principles of cancer registration contained within the 2nd Edition of 'Cancer Registration: Principles and Methods' published in 1991 are still valid and this publication still represents an authority on cancer registration, the methods of day-to-day registration and the statistical analysis of registry data have radically evolved over the last quarter century. An expanded and updated 3rd Edition of the book is being developed, in collaboration with IACR members, to benefit all registry staff working today in the 600 established registries worldwide. Two Editorial Board meetings reviewing chapters have taken place and the book comprising two parts – one on methods and uses of registration, the other on statistical methods, respectively – is being finalised.

The IACR fulfils a critical role as the professional society dedicated to fostering the aims and activities of cancer registries worldwide. With the emergence of the GICR, activities now underway in each region directly target current and future Association members. Ensuring greater convergence on training is a key area of activity, with the development of on-line learning modules linked to the contents of the book; these are being developed in collaboration with IARC/ETR.

Figure – Example of Essential TNM simplified staging system.



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Case Study #21: ROLE OF HUMAN PAPILLOMAVIRUS INFECTION AND OTHER CO-FACTORS IN THE AETIOLOGY OF HEAD AND NECK CANCER IN EUROPE AND INDIA – HPV-AHEAD

MTS areas: These activities contribute to IARC MTS Project Tree objectives 2.1.1 and 4.3

2.1.1 Advance understanding of the role of infectious agents

4.3 Provide the resources and infrastructure to support and enhance research

IARC Sections/Groups involved: led by Infections and Cancer Biology (ICB) with Genetic Epidemiology (GEP)

Alcohol consumption, smoking, poor oral hygiene, genetic factors, and infection with mucosal high-risk human papillomavirus (HPV) types are key risk factors for the development of head and neck cancer (HNC). Among the various HNC types, cancers of the lingual and palatine tonsils are most frequently associated with HPV infection. Although the overall incidence of HNC is decreasing in developed countries due to increasing awareness of tobacco and alcohol as risk factors for human carcinogenesis, the proportion HPV-positive HNCs has been steadily increasing in the USA and Europe. The Indian subcontinent has the highest HNC incidence in the world, accounting for one third of the global burden. Many etiological factors are involved in HNC development in the Indian population, however few studies reported the rates of HPV-positive cases.

In order to address this question IARC established a large multicentric study in Europe and India with the aim of evaluating the role of mucosal high-risk HPV types and other risk factors in the development of HNC in these two regions – HPV-AHEAD. The study is coordinated by IARC and involves 9 European and 7 Indian partners. Specifically, the main objectives of the HPV-AHEAD consortium were (i) to produce a formal systematic review on the available data and a comprehensive analysis of the descriptive epidemiology and time trends in HNC incidence and mortality in Europe and India and (ii) to conduct epidemiological studies in European and Indian populations in order to establish the overall proportion and type distribution of HPV-positive HNC at different anatomical sites in different geographical regions using multiple markers for HPV infections. In addition, HPV-AHEAD has been able to transfer technology to Indian research laboratories as well as to develop strategies for the training of European and Indian researchers in topics related to infections and cancers.

Initial results showed that the proportion of HPV-positive HNCs was lower in India than in Europe, and that HPV infection is mainly associated with oropharyngeal cancers, with only a small proportion HPV-positive oral and laryngeal cancers in both regions. Importantly, this research identified viral molecular markers that are differentially expressed in HPV-positive HNC in Europe and India, and demonstrated that the detection of HPV DNA alone was found to be insufficient proof for viral causality and could lead to misclassification of the HNC.

IARC's expertise in conducting international and multicentric studies was essential for the successful achievement of the goals of the HPV-AHEAD consortium. In addition to the scientific achievements, the HPV-AHEAD project made a significant contribution to the transfer of technologies and capacity for diagnostic tests for viral infections in India, through the organization of training courses in India on the role of infections in human carcinogenesis and the establishment of two HPV diagnostic laboratories in Mumbai and Trivandrum that are largely used for clinical and research studies.

Finally, HPV-AHEAD has been used by partners of the consortium as a model for the development of similar case-studies in India and Brazil that have been successful in mobilizing local funds for the research from the Indian Medical Research Council and EraNet, respectively.

Figure – HPV diagnostic laboratory at the Rajiv Gandhi Centre for Biotechnology (RGCB) in Trivandrum, India, established with support from the HPV-AHEAD project in partnership with local partners.

Case Study #22: THE BIOBANK AND COHORT BUILDING NETWORK (BCNET) AND THE B3AFRICA CONSORTIUM

MTS areas: These activities contribute to IARC MTS Project Tree objectives 4.1.2, 4.2.2 and 4.3.1

- 4.1.2 Deliver training courses, basic and advanced, in the areas of core competencies of the Agency
- 4.2.2 Improve and implement laboratory methods
- 4.3.1 Develop and maintain research platforms

IARC Sections/Groups involved: led by Laboratory Services and Biobank (LSB) with Education and Training (ETR)

A significant rise is expected of the cancer burden in low and middle income countries (LMICs) over the next decades simply due to population growth and ageing. However the genetic background of LMICs populations is frequently not represented adequately in cancer research and/or drug development studies. The result is solutions that are often not directly applicable or efficacious to populations in LMICs.

Biobanks contain collections of research-ready, well-annotated biological material from a given cohort and stored in an organized system with associated clinical data. The creation and successful maintenance of biobanks in LMICs can provide populations in these regions with the equitable opportunity to have their particular genetic and environmental make-up included in global research. The lack of biobanks, as part of the foundational research infrastructure, affects the long-term development of high quality cancer research within LMICs and the efficacy of subsequent public health policies.

To address this need IARC created in 2013 the Biobank and Cohort building Network (BCNet - http://bcnet.iarc.fr/) to support the establishment of biobanks in LMICs with appropriate sample and data management. The network, led by IARC with support from other international institutions, has since developed into a global focal point for LMIC biobanking, incorporating 34 institutions from 21 countries (Figure 1). BCNet is supported by the development of harmonised protocols, best practices and standards[1] and has established a catalogue program[2] to register the biological resources of its members, therefore providing global visibility for their collections.

IARC's unique international reach and BCNet's broad membership meant that international training opportunities could be organised on-site for Pathologists and Technicians on biobanking. These have taken place in Yogyakarta, Indonesia (2017, 2018, 2019)[10]; Abidjan, Cote d'Ivoire (2016)[11]; and Cairo, Egypt (2016, 2018, 2019).[12] These BCNet training courses coordinated by IARC, reflect

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[10] In partnership with Universitas Indonesia,Jakarta; Universitas Gadjah Mada, Yogyakarta; and the Indonesian Medical Education Research Institute, Faculty of Medicine (http://imeri.fk.ui.ac.id/).
[11] In partnership with the Institute Pasteur Côte d'Ivoire and the International Academy of Pathology-West African Division.
[12] In partnership with the National Cancer Institute, the Children's Cancer Hospital in Egypt and co-funded by USA-CGH and the ADOPT-BBMRI Project (EU-H2020 676550).

areas of core competency of the Agency, including Laboratory and Data Standards; Ethical, Legal and Social Issues (ELSI); Quality Control and Information Technology (IT)[3].

Additionally, through its participation in the EU-sponsored research consortium Bridging Biobanking and Biomedical Research across Europe and Africa (B3Africa)[13], BCNet has acted as the backbone bringing the LMIC institutions into the EU funded projects, as well as providing online educational material and cloud-based IT infrastructure to BCNet partners. In conjunction with the training courses this activity supports the aim of maintaining laboratory and computing services within IARC and across the BCNet, while creating the conditions for further funding opportunities.

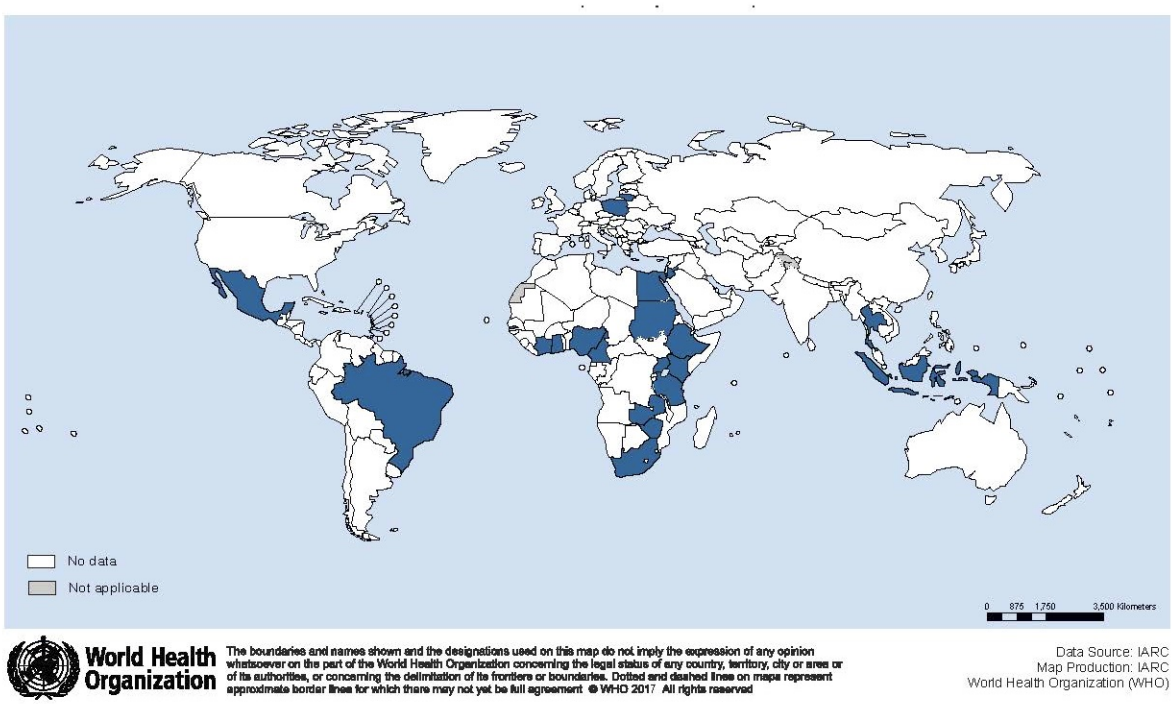

Figure 1: Map showing the BCNet membership as of August 2018

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[13] Funded by the EU Horizon2020 research and innovation programme, grant agreement No 654404.

Case Study #23: TRAINING THE MASTER TRAINERS FROM FRANCOPHONE AFRICA ON CERVICAL CANCER SCREENING, DIAGNOSIS AND MANAGEMENT OF CERVICAL CANCER PRECURSORS

MTS areas: These activities contribute to IARC MTS Project Tree objectives 3.2, 4.1.2 and 5.3.1

- 3.2 Enhance the implementation of cancer prevention and control programmes
- 4.1.2 Deliver training courses, basic and advanced, in the areas of core competencies of the Agency
- 5.3.1 Create and maintain key strategic partnerships with national, regional and international organisations

IARC Sections/Groups involved: Led by Screening (SCR) with contributions from Education and Training (ETR)

Supporting human resource development for cancer research on prevention and early detection in LMICs is one of the key mandates of IARC. The Agency, in close partnership with Morocco's Lalla Salma Foundation for Cancer Prevention and Treatment (LSF), ran a series of training courses for master-trainers from Morocco, Senegal, Ivory Coast, Gabon and Chad in cervical cancer screening, colposcopy and treatment of cervical pre-malignancies to develop research capacity and assist the implementation of cervical cancer screening programs in these Francophone African countries. The cascading impact of the training on the work force development was immediate, since the trained master-trainers trained more health providers after returning to their respective countries.

The week-long training courses were organized in September 2016, May 2017 and February 2018, each attended by approximately 20 trainees. The first course was aimed at gynaecologists from Morocco only and the other two courses had trainees from Morocco as well as the other Francophone countries. All the trainees were selected and recommended by the Ministries of Health of their respective countries. While the faculty for the first two courses were from France and India, the Moroccan master-trainers trained in the first course served as the faculty for the third course, thus initiating a 'south-south' partnership.

A blended combination of different training techniques (e-learning, hands-on practical workshop and facility tour) was tailored to provide both theoretical and practical knowledge to the participants. The e-learning session comprised of a series of pre-recorded lectures made available online to the participants through a dedicated platform on the IARC website. After successful completion of the online lectures the participants were allowed to attend the practical sessions organized at one of IARC's collaborating sites in India (Nargis Dutt Memorial Cancer Hospital, Barshi). The practical sessions included demonstration of the techniques of visual inspection with acetic acid (VIA) screening, colposcopy, treatment of premalignant lesions with cryotherapy, thermal ablation and large loop excision of the transformation zone (LLETZ). The trainees were allowed to perform the procedures under supervision and an objective competency evaluation was performed at the end of the training. All participants that successfully completed the course were

given a certificate and provided with power-point presentations, repository of images and other teaching materials.

The impact of this initiative was exponential: master-trainers from Morocco trained a large number of nurses and gynaecologists in the country to perform VIA and colposcopy respectively and thus contributed to strengthen the national cervical cancer screening program. The master-trainers from Senegal and Ivory Coast further trained total 64 nurses and gynaecologists from the public health services in their respective countries. The trained providers have already initiated cervical cancer screening in Dakar and Abidjan in the primary healthcare settings. IARC and LSF have supported these countries with equipment, data collection tools and electronic databases to sustain the cervical cancer screening activities.

IARC will also provide assistance to evaluate the initial pilot programs on VIA screening and treatment in these countries. This work is integrated in the framework of a broader research programme, the 'Care4Afrique' project, evaluating the implementation and scaling up of cervical cancer screening and treatment in Francophone Africa.

Figure – Online training resource developed by the Screening Group

Figure – Training master-trainers from Francophone African countries in Barshi, India, Feb. 2017

Case Study #24: IARC'S PARTICIPATION IN IMPACT REVIEW MISSIONS

MTS areas: These activities contribute to IARC MTS Project Tree objectives 1.2, 3.2 and 5.3

1.2 Support improved coverage and quality of cancer registration, particularly in low and middle-income countries

3.2 Enhance the implementation of cancer prevention and control programmes

5.3 Create and maintain key strategic partnerships with national, regional and international organisations

IARC Sections/Groups involved: Cancer Surveillance Section (CSU) and Early Detection and Prevention Section (EDP)

The Integrated Missions of PACT (imPACT Reviews) are detailed assessments of a country's cancer control capacity and needs, with the aim of supporting low- and middle-income countries (LMICs) in their efforts to develop effective comprehensive cancer control programmes. They are coordinated by the Programme of Action for Cancer Therapy (PACT) of the International Atomic Energy Agency (IAEA), and conducted jointly with WHO and IARC.

The missions consist of site visits of cancer control facilities and services, together with meetings with key local stakeholders and government officials, carried out by an international multidisciplinary team of experts. IARC nominates the experts in 'Cancer Registration and Surveillance' and 'Prevention and Early Detection', most often IARC staff from one of the relevant Sections. The outcome of the imPACT Reviews is a Mission Report submitted to the local Ministry of Health, jointly endorsed by IAEA, WHO and IARC, providing a detailed summary of the findings and a series of recommendations.

Since the establishment of the programme in 2005 over 100 LMICs have received an imPACT Review, of which approximately 2/3 included the participation of IARC-nominated experts.

Since January 2016 IARC staff or IARC-nominated experts participated in imPACT reviews in the following countries:

2016	2017	2018
Belarus Honduras Kazakhstan Kenya Liberia Paraguay Sierra Leone	Belize Burundi Congo (Republic of the) Swaziland Togo	Indonesia Ukraine Macedonia (FYR of) Mexico Guyana Ecuador

The Agency makes a unique contribution to the imPACT Review programme: IARC-nominated experts are valued for their strong technical expertise combined with experience of working in LMIC settings; moreover, IARC, together with WHO and other partners, has participated in expert meetings at IAEA to periodically review imPACT methodology.

In turn, the imPACT Review missions have provided valuable insight into potential opportunities for research collaborations in the countries visited in priority areas of interest for IARC, together with contacts with local scientific and technical partners and government decision makers. These contacts have been instrumental in the implementation of some of the Agency's programmes directly linked to supporting the development of infrastructure and capacity for cancer prevention and control.

As international agencies, IARC together with IAEA and WHO, have a mandate to provide advice to national governments, thus maximizing the potential impact of their technical expertise. As one of the three UN Agencies jointly responsible for the imPACT Review missions, IARC has influenced the cancer control programmes of over 70 LMICs, by providing advice and support to the governments to prioritise evidence-based cancer control interventions and investments, reflecting one of the overarching goals of the IARC Medium-Term Strategy 2016-2020, of supporting the translation of research and technical expertise to public health recommendations for cancer prevention and control.

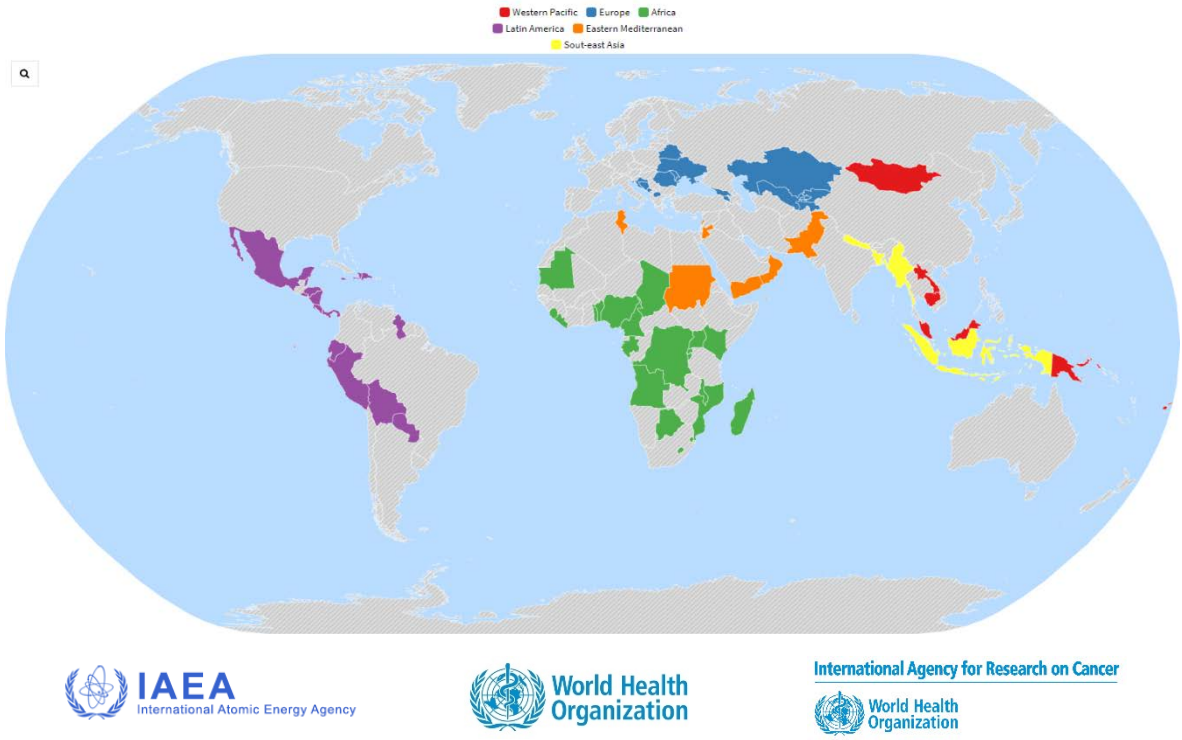


Figure – Map of countries in which IARC nominated experts participated in imPACT missions coordinated by IAEA, since the establishment of the programme in 2005.
Number of countries by WHO Region: Africa – 22; America – 15; Europe – 14; Eastern Mediterranean – 7; Western Pacific – 6; South-east Asia – 4.

Case Study #25: SUPPORTING INTRODUCTION OF COLORECTAL CANCER SCREENING IN DEVELOPING COUNTRIES WITH RISING BURDEN OF THE CANCER

MTS areas: These activities contribute to IARC MTS Project Tree objectives 3.2.1, 4.1.2 and 5.3.1

- 3.2.1 Identify factors influencing the effective implementation of primary and secondary prevention programmes
- 4.1.2 Deliver training courses, basic and advanced, in the areas of core competencies of the Agency
- 5.3.1 Create and maintain key strategic partnerships with national, regional and international organisations

IARC Sections/Groups involved: led by Screening (SCR) with contributions from Nutrition and Metabolism Section (NME)

The Agency provides technical assistance to colorectal cancer screening demonstration projects in Morocco, Iran and Saudi Arabia, with the aim to assess the feasibility, safety, acceptability and cost-effectiveness of faecal immunochemical test (FIT) based screening. All these countries in the WHO Eastern-Mediterranean region have reported a growing burden of colorectal cancer. The demonstration projects utilize local human resources and routine health care system facilities and are supported by the Ministries of Health of the respective countries.

Prior to the launch of the program in Morocco in May 2017, the Agency organised a 3-day training course of the nurses and general practitioners from 10 primary health centres in urban and semi-urban areas of Morocco that would be taking part in the demonstration project. IARC assisted the national collaborators in drafting the protocol, designing the data collection forms, developing mechanisms to track the screen positive individuals and developing the online database for data management with a view to subsequent scientific evaluation of the implementation. To date, approximately 9000 men and women aged 50 to 75 years were screened by FIT at the primary health centres and the screened positive individuals were referred for colonoscopy at the National Oncology Centre of Rabat. IARC is working closely with the Moroccan collaborators for regular site supervision and for monitoring the progress of recruitment and different process measures. The final outcomes will be the detection rate of colorectal cancer and high grade adenomas, the acceptability and safety of the interventions and the satisfaction level of the participants.

The expertise developed with Morocco is serving as a model for the establishment of similar colorectal cancer screening demonstration projects in the other countries: in Iran the Agency is assisting in the implementation of a demonstration project in Teheran, which aims to screen 5000 participants aged 50 to 70 years at 10 primary health centres (5 in urban and 5 in rural settings) with FIT tests; in Saudi Arabia the demonstration project will evaluate a quantitative FIT test to screen 6000 men and women between 45 and 75 years, and includes colonoscopy for a group of 10% randomly selected FIT negative individuals (in addition to the FIT positive individuals) that will allow to estimate the accuracy of quantitative FIT test using different cut-offs.

Finally, the Agency is taking advantage of the colorectal screening infrastructure established in these three countries to implement a gut microbiome profiling study in normal as well as in the diseased individuals. The aim is to assess the gut microbial composition and diversity and assess interactions between lifestyle, the gut microbiota and colorectal adenomas and cancers.

The impact of these projects goes well beyond the immediate results of the screening demonstration programmes: IARC is helping to create a research platform using the existing health services infrastructure by supporting the development of technical capacity and expertise amongst local healthcare personnel; and the close collaboration with the Ministries of Health in the three countries will inform the development of evidence-based policy on the introduction of colorectal cancer screening in the next national cancer plans. Furthermore the recent IARC Handbook on Cancer Prevention focusing on cancer screening provides a valuable resource to countries considering the introduction of colorectal cancer screening.

Figure – The front page of the National Cancer Control Plan, Morocco (2010–2019)

Figure – Nurses being trained to perform FIT test for colorectal cancer screening in Morocco, March 2017

Case Study #26: ESTIMATING CANCERS RELATED TO LIFESTYLE AND ENVIRONMENTAL FACTORS IN FRANCE: SUPPORTING MASS HEALTH CAMPAIGN AND NATIONAL CANCER CONTROL PLAN

MTS areas: These activities contribute to IARC MTS Project Tree objectives 1.1, 3.2 and 5.3

1.1 Improve and expand reporting of descriptive cancer statistics
3.2 Enhance the implementation of cancer prevention and control programmes
5.3 Create and maintain key strategic partnerships with national, regional and international organisations

IARC Sections/Groups involved: led by the Cancer Surveillance Section (CSU) with contributions from Environment and Radiation Section (ENV), Nutrition and Metabolism Section (NME), IARC Monographs Group (IMO) and Infections and Cancer Epidemiology Group (ICE)

As noted in the IARC MTS, expertise in the development of Population Attributable Fractions (PAF) for major risk factors (e.g. obesity, alcohol, tobacco and other carcinogenic agents identified through the Monographs) has led to multiple and ongoing collaborations across Sections.

While much progress has been made in identifying the causes of human cancer, the contribution of established risk factors to the burden of cancer differs by country with patterns of exposure varying according to environmental, socioeconomic, cultural and other factors. Analyses of the proportion of cancers attributable to major cancer risk factors within the population of a specific country are particularly informative, providing the evidence for prioritising cancer prevention measures and guiding cancer prevention policy.

In France, previous work on the causes of cancer in 2000 reported that 35% of cancers were probably preventable. Since then, new evidence on the carcinogenic effects of additional risk factors such as red and processed meat, exposure to diesel and air pollution have emerged. This multi-partner project led by IARC and funded by the French national cancer institute (INCA) provided the opportunity to deliver a comprehensive set of up-to-date estimates of the proportion of cancers attributed to past exposure to various lifestyle and environmental risk factors in France.

In order to ensure the integration of the most up-to-date evidence on the causes of cancer – including evaluations by the *IARC Monographs* – using state-of-the art methods, IARC coordinated the work of an international team comprising 70 experts from France, IARC and globally. The project was built around thirteen working groups on each of the major risk factor categories that guided the retrieval and assessment of the data by a core team of IARC scientists. A steering committee chaired by IARC involving representatives from IARC and from major French national health agencies and research centres and an international advisory committee oversaw the project to ensure the production of high quality estimates that are consistent throughout the various risk factors groups.

This project contributed to a better understanding of the causes of cancer in France and the relative contribution of each risk factor on the current burden of cancer. In 2015, 41% (or 142,000 of 346,000) of all new cancers diagnosed in France could be attributed to the aforementioned risk

factors. The numbers and PAF were slightly higher in men than in women (84,000 versus 58,000 cases and 44% versus 37%, respectively). Smoking (PAF: 20%), alcohol consumption (PAF: 8%), dietary factors (PAF: 5%) and excess weight (PAF: 5%) were the most important factors.

The results have been widely communicated, and have been used by the national health agencies to communicate public health messages with the goals to reduce exposure to cancer risk factors. Further, the results will be used to inform the forthcoming National Cancer Plan in France to better target prevention action; it also serves to fund prevention actions identified as crucial to reduce the future burden of cancers. The approach taken provides a model which could be used in other national exercises.

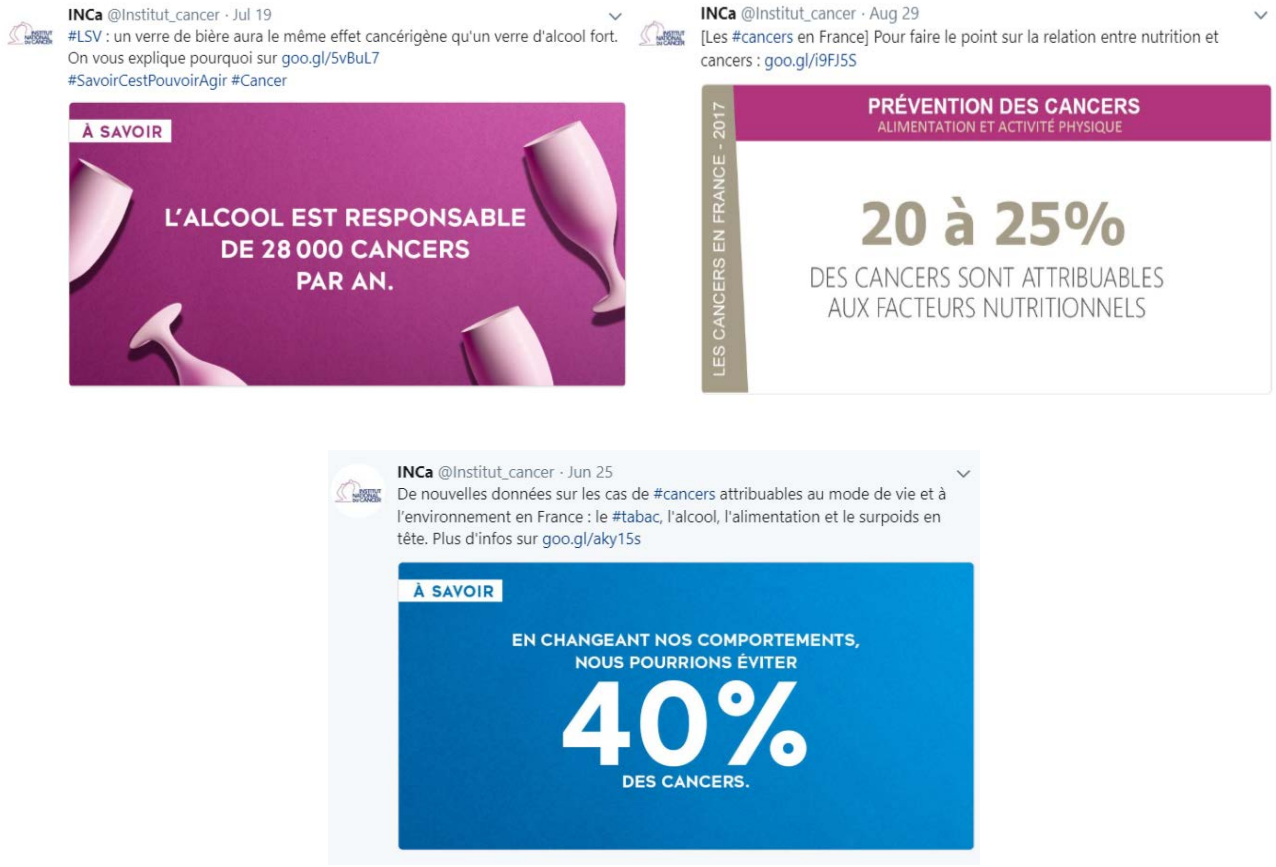


Figure – Examples of public health messages on cancer prevention based on the results of the study on PAF in France, by the *Institut National du Cancer* (INCa)

Case Study #27: EVALUATION OF IMPACT OF HPV VACCINATION PROGRAMMES IN RWANDA AND BHUTAN

MTS areas: These activities contribute to IARC MTS Project Tree objectives 3.1.1, 3.2.1, 4.1 and 5.3

- 3.1.1 Analyse the effectiveness of primary cancer prevention strategies
- 3.2.1 Identify factors influencing the effective implementation of primary and secondary prevention programmes
- 4.1 Increase human resources for cancer research
- 5.3 Create and maintain key strategic partnerships with national, regional and international organisations

IARC Sections/Groups involved: led by Infections and Cancer Epidemiology (ICE) with contributions from Infections and Cancer Biology (ICB)

HPV vaccination is expected to hugely impact the global cervical cancer burden, but this effect will not be seen fully on the incidence of cervical cancer for at least 20 years. In the meantime, population-level evidence of vaccine effectiveness against HPV infection is crucial to encourage national planners to implement and sustain HPV vaccination programmes. Indeed, compared to efficacy seen in clinical trials, vaccine effectiveness in real-life settings might be lower (e.g. sub-optimal vaccine delivery/coverage), or higher (e.g. strong herd immunity). This requires implementation research.

Data on effectiveness is increasingly available from high-income countries, but much less is available from LMICs. Indeed, WHO does not recommend impact monitoring as a pre-requisite for LMICs implementing HPV vaccine, given that it requires specific research expertise as well as substantial time and cost, but instead advises that impact evaluation in some sentinel settings is important to serve as an evidence model.

IARC is at the forefront of assessing HPV vaccine effectiveness in sentinel settings through long-standing collaborations with successful early implementing LMICs, namely Bhutan (vaccinating 12-to-18 year old girls since 2010) and Rwanda (vaccinating 12-to-15 year old girls since 2011). This project has published preliminary results on HPV vaccine impact since 2015, but continues to monitor vaccine effectiveness as vaccinated cohorts grow older and become sexually active.

IARC is collaborating directly with Ministries of Health in Bhutan and Rwanda, and, as an international institution, is well placed to coordinate multi-LMIC epidemiological studies that are embedded in national public health programmes. Furthermore, IARC has a unique experience in mapping global HPV epidemiology, through more than 25 years of undertaking HPV and cervical cancer research worldwide. To facilitate this implementation research, IARC convenes a multidisciplinary set of local investigators from LMICs and required expertise from high-income countries (e.g. in HPV testing and cytohistopathology).

HPV vaccination is the principal tool for reaching the WHO target for cervical cancer elimination. As one of the few projects evaluating the effectiveness of HPV vaccination in LMICs this programme of work has potentially a major impact in this flagship initiative led by WHO.

Education and training form a key part of this project, including the development of future cancer researchers through co-supervision of Masters and PhD students in Rwanda, and cultivation of networks to develop additional cancer research programmes (e.g. evaluation of HPV-based screening; HIV and cancer).

Figure – Information session on HPV vaccination, Rwanda 2017

Figure – HPV vaccination programme, Bhutan 2017

Case Study #28: THE GLOBAL INITIATIVE FOR CANCER REGISTRY DEVELOPMENT – GICR: BUILDING REGIONAL NETWORKS TO STRENGTHEN COUNTRY CAPACITY

MTS areas: These activities contribute to IARC MTS Project Tree objectives 1.2, 4.1 and 5.3

1.2 Support improved coverage and quality of cancer registration, particularly in low and middle-income countries

4.1 Increase human resources for cancer research

5.3 Create and maintain key strategic partnerships with national, regional and international organisations

IARC Sections/Groups involved: led by the Cancer Surveillance Section (CSU) with contributions from Education and Training Group (ETR)

The Global Initiative for Cancer Registry Development (GICR) is the first international strategy to inform cancer control policy through better registry data. Launched in 2011 by IARC, the GICR is a partnership based on the commitment of leading cancer organizations to address inequities. The aim is to build in-country capacity to collect their own local cancer data, synthesise and disseminate findings so that targeted actions can be taken to tackle the rising cancer burden. Six IARC Regional Hubs for Cancer Registration have been established to support Africa, Asia, the Caribbean, Latin America and Oceania. Each Hub acts as the main point of contact for countries within its catchment area to assist and coordinate GICR activities. To further increase the availability of assistance, and to bring it closer to those who need it, a number of IARC-GICR Collaborating Centres have been established to work with each Hub.

Training in cancer registration is in high demand. The model used to address needs is a global support network, termed GICR*Net*. Teams of designated IARC Regional Trainers are being equipped with educational resources to work alongside colleagues in nearby countries to transfer their knowledge and provide ongoing guidance. Experts from each of the Hub regions have been selected and trained by IARC in specific subject areas. The International Association of Cancer Registries (IACR), the professional body that governs the field, is a key partner in this activity. International standards, jointly developed and endorsed by IACR, form the basis of technical references that are used by the GICR in training.

Similarly, access to learning materials and their availability in local languages are challenges in low resourced settings. To help reduce barriers, the GICR is producing a series of on-line, e-learning modules based mainly on the forthcoming third edition of the IARC publication *Cancer Registration: Principles and Methods*.

To complement formal training, the GICR Mentorship and Twinning Programme will provide opportunities for knowledge transfer through peer-to-peer exchanges. The goal is to build local capacity by matching established cancer registries with those less developed within the same region to work on specific, in-depth areas of need.

The GICR is a programme of coordinated activities that will ultimately save lives. This vision is built on the understanding that an accurate measure of the burden drives improvements in health care systems through national cancer control planning. Through the GICR, a new generation of skilled health professionals are being trained to convert data into information that policy makers, clinicians and researchers can more easily use. Barriers to the collection and use of cancer incidence and survival data are being eliminated. Decisions in prevention, screening and treatment programs are being guided by stronger evidence. Determinants of cancer causes and diagnosis will be better understood by benchmarking comparisons between populations. The development of new electronic tools will reduce costs and modernize health information systems away from paper-based approaches. Over time, these activities will translate to better health, economic and social outcomes.

Figure – GICR goals and activities

Case Study #29: INFORMED CANCER CONTROL PLANNING: MAKING THE RIGHT INVESTMENT USING AN INTERACTIVE PLATFORM

MTS areas: These activities contribute to IARC MTS Project Tree objectives 1.1.1, 3.1, 3.2 and 5.3

- 1.1.1 Expand the descriptive analyses of cancer incidence, mortality, prevalence and survival regionally and worldwide
- 3.1 Enhance understanding of interventions for cancer prevention and control
- 3.2 Enhance the implementation of cancer prevention and control programmes
- 5.3 Create and maintain key strategic partnerships with national, regional and international organisations

IARC Sections/Groups involved: led by Prevention and Implementation (PRI) with contributions from Cancer Surveillance Section (CSU).

The economic impact of cancer is significant and increasing. In 2010, the total annual economic cost of cancer was estimated at approximately US$ 1.16 trillion, threatening health budgets and economies at all income levels as well as causing financial catastrophe for individuals and families. Cancer health planners are tasked with identifying strategic priorities that maximize the return on investments resulting in reduced burden of cancer, improved health and financial protection. Cancer control programmes must be developed within the context of health systems and tied to sustainable funding. While various models and tools have been developed to assist with cancer planning, there are currently no tools that can assist policymakers identify priorities based on considerations of impact and cost-effectiveness using a health systems approach.

World Health Assembly Resolution 70.12 (2017) urges WHO, and IARC, to provide evidence on priority, cost-effective cancer control interventions and to support governments to promote universal access to cost-effective care for the integrated management of cancers. In response, WHO and IARC are jointly developing a tool that evaluates the impact, cost and feasibility of selected cancer interventions, adjusted for context-specific health system capacity to assist policy makers obtain the best value for money in health spending.

The project aims to improve our understanding of the impact, cost, feasibility and cost-effectiveness of a wide range of cancer control interventions for approximately 10 different cancers for LMICs, and inform countries on the most efficient, effective and sustainable cancer control interventions taking into account their health system context. This objective will be achieved through two deliverables and validated by in-country pilot workshops in a number of selected countries. The two deliverables are (i) an interactive platform that models the impact and costs associated with priority cancer control interventions across the cancer continuum and (ii) an investment case for cancer prevention and control.

Methods include a comprehensive review of existing costing tools and macroeconomic data relevant to cancer prevention and control; identification of modelling strategies to estimate the burden of cancer; and identification of key cancer prevention and control programmes and care pathways. The deliverables will align with existing economic tools and prior cancer cost-

effectiveness analyses. In particular, the WHO-CHOICE (CHOosing Interventions that are Cost-Effective) methodology will be used and an interactive platform that links goals of strategic plans to cost estimates using OneHealth Tool methodology will be developed.

The project is being developed as a collaboration between IARC and the WHO headquarters office in Geneva (WHO/HQ). IARC was involved in the design of the study, and is actively participating in all its components. The project also strengthens collaboration and information sharing between WHO/HQ and IARC in the field of priority setting and health technology assessment.

In terms of the impact more broadly, the provision of expertise for international policy development and documenting the global economic burden and impact of cancer is a key priority to PRI and IARC. The project will assist policy makers obtain the best value for money in health spending by providing a business plan with priority cancer interventions informed by context-specific health system capacity. Furthermore, the interactive tool will enable the formulation and testing of novel research hypotheses of importance to cancer control, and assessing the impact of rapidly evolving cancer technologies using a standardized platform.

Case Study #30: CANCER PREVENTION EUROPE – CPE

MTS areas: These activities contribute to IARC MTS Project Tree objectives 4.3 and 5.3

- 4.3 Provide the resources and infrastructure to support and enhance research
- 5.3 Create and maintain key strategic partnerships with national, regional and international organisations

IARC Sections/Groups involved: Environment and Radiation Section (ENV) and Director's Office (DIR)]

Cancer Prevention Europe (CPE) is an international multidisciplinary consortium of European research institutes, organisations and networks of excellence that was created in 2018 under an initiative of IARC. The overall objective is to shape and advocate for world class prevention research in Europe that will inform effective cancer prevention guidelines and policies at national and international level. Drawing from previous experience from the European platform for translational cancer research (EurocanPlatform) and with the focus on expanding preventive interventions, taking as a starting point the measures summarised in the 4th edition of the European Code against Cancer, CPE will aim to reduce cancer morbidity and mortality through prevention.

CPE will be broad in scope covering a spectrum of research from behavioural and laboratory science to policy research, as well as dissemination of the best evidence, quality indicators and practices. Assessment of the cost-effectiveness of different interventions, in relation to costs of treatment, care and productivity loss will be a core component of the initiative. Primary, secondary and tertiary prevention will be encompassed and emphasis will also be placed on the research evaluation and advocacy dimensions of the prevention agenda. CPE will offer an integrated infrastructure capable of assuring high quality research and each CPE partner institution will bring specific expertise in cancer prevention research as well as in communication and informing policy and practice.

The agenda for CPE includes (1) research into optimising the implementation of known preventive strategies, (2) dissemination and research translation to inform policy and practice (3) the identification of novel targets for prevention and (4) promote the case for greater research investment in prevention in Europe. Specific research activities for CPE encompass the following areas: cancer registration; cancer aetiology (including recurrence); development and evaluation of preventive interventions (primary, secondary, tertiary); health economics and implementation research to enhance the effectiveness of intervention programmes. These will be supported by a range of platforms, networks and infrastructures and draw together a wide network of partners. Training and capacity building will be integral to the initiative.

IARC, with its extensive expertise in coordinating inter-disciplinary projects across countries and organizations, hosts the Scientific Secretariat of the CPE consortium and will help support CPE priority actions within a 5-year Strategic Plan.

Successful coordination of cancer prevention requires long-term vision, a dedicated research agenda and funding, as well as a sustainable infrastructure and cooperation between countries and programmes. CPE offers the opportunity to fill gaps in the evidence-base for prevention,

shaping cancer research agenda in Europe and beyond, to avoid common pitfalls in implementation and to share capacity for research training and quality improvement.

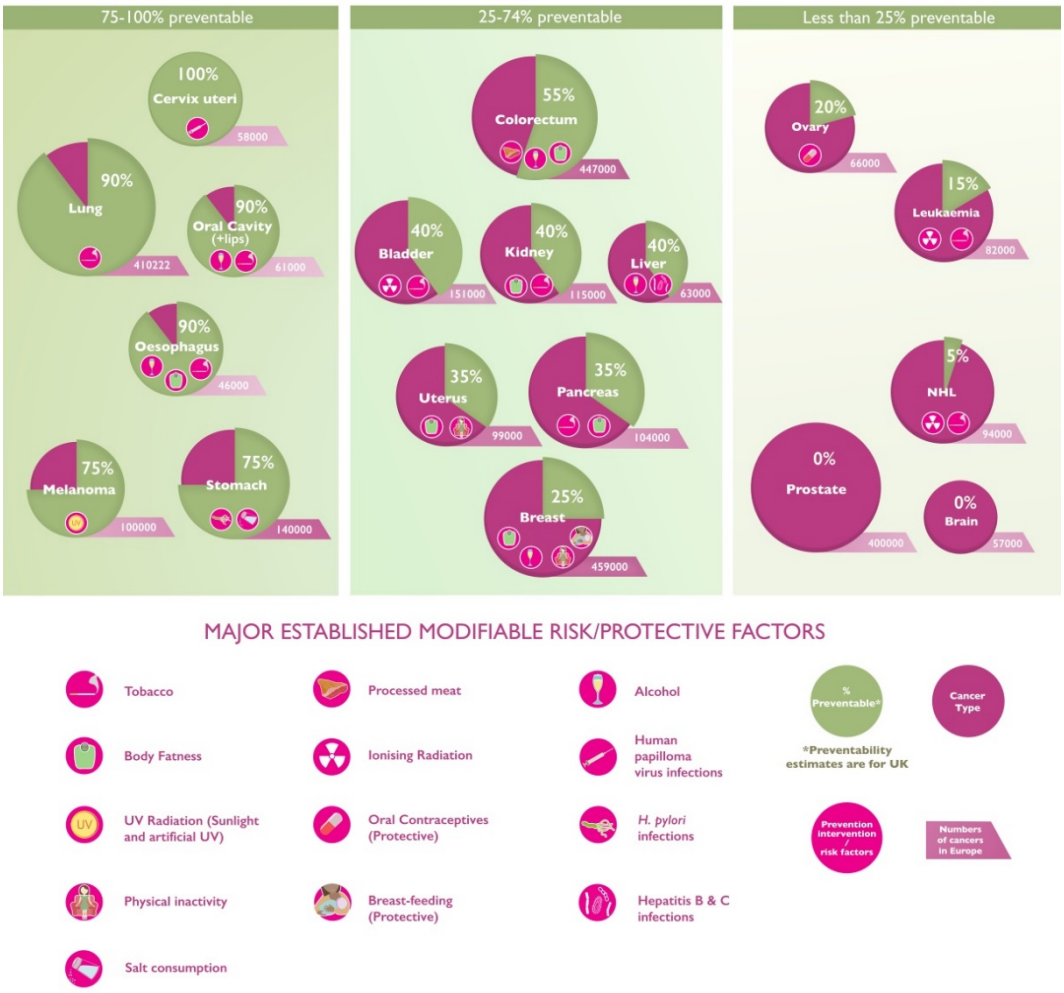


Figure – Most common cancers in Europe: estimated incidence for 2012 and proportion potentially preventable from changes in currently established risk and protective factors.

Case Study #31: THE WHO CLASSIFICATION OF TUMOURS – WCT

MTS areas: These activities contribute to IARC MTS Project Tree objectives 1.3 and 5.4.1

1.3 Improve WHO tumour classification to inform cancer registration, research and treatment

5.4.1 Effectively communicate and disseminate the work of the Agency

IARC Sections/Groups involved: WHO/IARC Classification of Tumours (WCT)

The WHO Classification of Tumours series based at IARC is also commonly referred to as the WHO Blue Books. The Blue Books are a prime example of the broad impact of IARC's work, illustrating both an influence on practice via consensus reports developed by scientific experts and an ability to leverage in-kind contributions from those experts with the common goal of producing "public goods" for the wider cancer community.

The recently established Blue Books editorial board consists of 20 standing members nominated by pathology organizations worldwide, with an additional 12-16 pathologists per individual volume selected on the basis of their publication record in the area. In addition, each volume typically receives contributions from 150-200 authors, representing around 1800 authors over the course of each new Edition of 10 or 11 volumes. These contributions come without any honorarium or other payment to co-authors, other than travel expenses for face-to-face meetings of the editorial board and demonstrate the ability of IARC to convene world leading experts to provide an essential support to cancer control internationally.

In terms of technical content of the Blue Books, the definitive diagnosis and classification of individual cancers not only underpins the care of all cancer patients, but is also critical for research into cancer causation, prevention, diagnosis, and treatment. In the past, this has been the preserve of histopathology, but in recent years a wealth of new information has been generated from other sources, notably from genetics and molecular pathology, as well as from computational methods and clinical imaging. In many instances integration of this data with the histopathology findings is critical for definitive disease classification. There is therefore an urgent need to integrate these facets of diagnosis into cancer classification worldwide.

The development of a new classification of melanoma, as part of the Skin tumours WHO Blue Book (figure 1), provides a good illustration of the reach of this work. There have been major developments in our understanding of the genetic basis of melanoma, and in treatments based on this knowledge. The new volume introduces a pathway-based classification of melanoma, which explains many of the differences in pathology and clinical behaviour between the different types. That said, the primary diagnostic tool remains histopathology, and the various histopathological patterns recognized by pathologists are now very clearly shown also to be different by genetics.

The WHO Classification of Tumours is essential to the internationally standardised diagnosis of benign and malignant tumours in every organ, and is updated periodically to reflect the latest knowledge and understanding of these tumours. IARC as the cancer agency of WHO is ideally positioned to provide leadership and coordinate this work; furthermore, in some instances the research conducted by the Agency contributes directly to the classification, as demonstrated in recent years for brain cancers and neuroendocrine tumours.

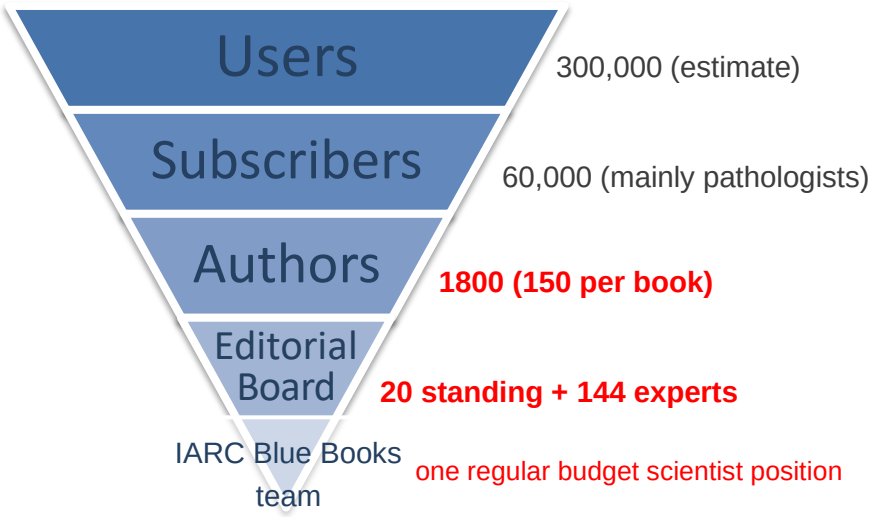
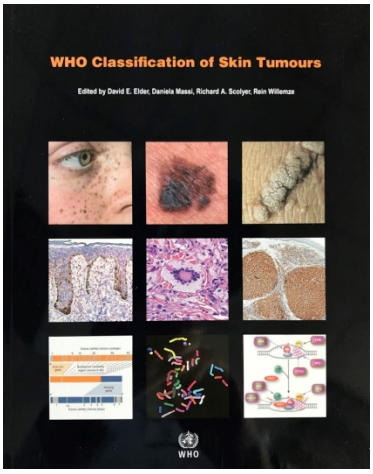


Figure – IARC/WHO Blue Books – in-kind contributions by the global scientific community



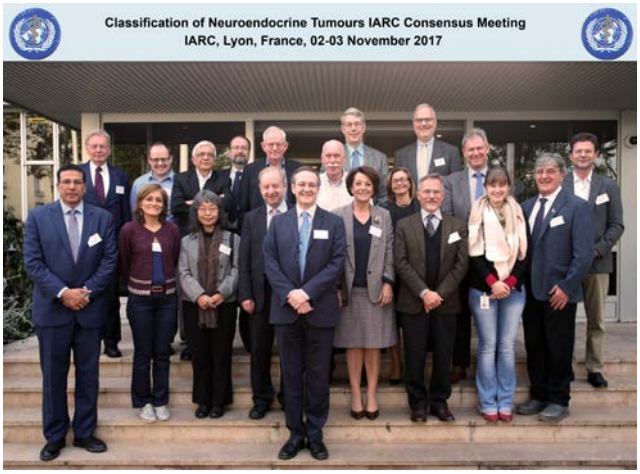


Figure – The 4th Series WHO Blue Book for Skin Tumours, published September 2018.

Case Study #32: CANREG5 – FREE, OPEN SOURCE CANCER REGISTRY SOFTWARE

MTS areas: These activities contribute to IARC MTS Project Tree objectives 1.2 and 4.1.2 and 4.3

- 1.2 Support improved coverage and quality of cancer registration, particularly in low and middle-income countries
- 4.1.2 Deliver training courses, basic and advanced, in the areas of core competencies of the Agency
- 4.3 Provide the resources and infrastructure to support and enhance research

IARC Sections/Groups involved: Cancer Surveillance Section (CSU)

Electronic data entry, management and analyses are key functional requirements for cancer registries to produce high quality data. Combining these features into one tool can be challenging, particularly in lower-resourced settings. To assist cancer registries in these countries IARC together with the International Association of Cancer Registries (IACR) developed CanReg. First released in 1986, the latest version, CanReg5, was launched in 2010. To ensure a broad base of users, the system allows for flexibility through the customization of variables, layouts and the ability to easily be adapted into the local language of the registry. Designed for users with rudimentary IT skills, it operates on environments with minimal hardware requirements while preserving security functions to protect access to the data. Worldwide, over 100 countries have used CanReg.

Users of CanReg5 have at their disposal a full suite of data quality features. Modules in CanReg5 for data entry and management incorporate essential quality controls. Automated edit checks increase compliance with international standards and comparability. Additional built-in features include duplicate searches, tables/figures to assess data quality and the use of mandatory fields that are flagged if not entered.

A core strength of CanReg5 is the support that is provided. Complementing user manuals and help functions, dedicated staff at IARC are available to assist registries with queries and delivering training. Staff at IARC have responded to over 300 CanReg5 queries per year and have contributed to over 60 courses regarding the software.

Experienced users have also participated in supporting colleagues. This approach was recently reinforced through resources available through GICR*Net*, which under IARC's Global Initiative for Cancer Registry Development programme includes a formal network of regional CanReg5 experts and series of instructional webinars.

Feedback from cancer registries is used to prioritize enhancements to address problem areas or add new features within CanReg5. Experts in GICR*Net* have helped to significantly improve reporting. High-quality graphical outputs can be generated by users with options to save the results in a variety of formats. Users can also edit figures and tables, along with the ability to customize their analyses. A standard cancer registry report is one example of the type of output that can be produced. Text and guidelines for registries to tailor specific sections of the report accompany statistical information, making possible real-time reporting.

The software is freely available so that individual cancer registries do not need to bear the costs of development. Thus CanReg5 proves a means to collect, store and analyse data – leading to a greater comparability and dissemination.

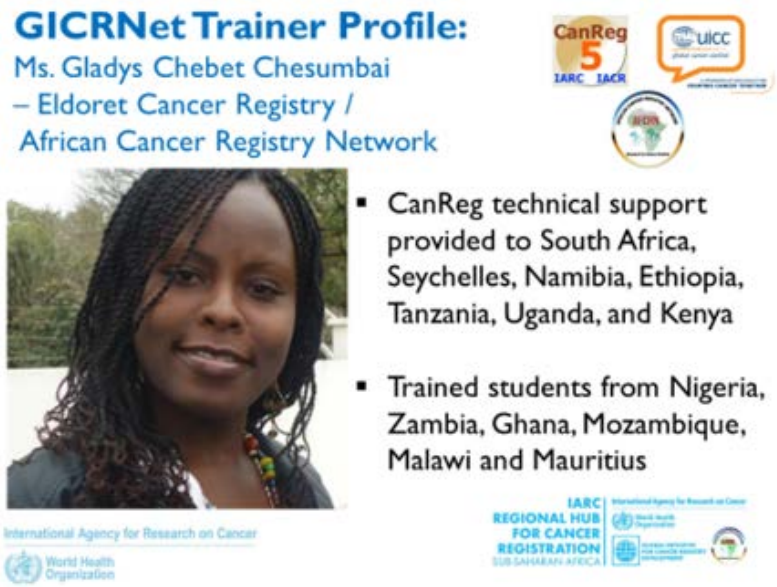


Figure – GICRNet - Network of regional CanReg5 experts and series of instructional webinars.

Case Study #33: IARC BIOINFORMATICS PIPELINES

MTS areas: These activities contribute to IARC MTS Project Tree objectives 4.2.1 and 4.3

4.2.1 Improve and implement epidemiological, statistical and bioinformatics methods

4.3 Provide the resources and infrastructure to support and enhance research

IARC Sections/Groups involved: led by Genetic Cancer Susceptibility (GCS) with contributions from Genetic Epidemiology (GEP), Molecular Mechanisms and Biomarkers (MMB), Epigenetics (EGE), Infections and Cancer Biology (ICB).

The field of computational biology has an important and increasing role in cancer research. Technological advances like high-throughput sequencing have been driving the development of analytical and computational methods to allow scientific insights to be drawn from these complex and often multifaceted datasets. This series of non-trivial data processing steps, designated "bioinformatics pipelines", can be difficult to implement and reproduce. A simple user-friendly framework to allow collaborative implementation of bioinformatics pipelines was developed at IARC (see Figure). Contributions to this community come from bioinformaticians and early career scientists from multiple scientific and administrative groups across IARC. All of the bioinformatics pipelines developed are shared as open-source projects through the IARC GitHub page (https://github.com/IARCbioinfo) for the benefit of the wider scientific community.

The framework was designed to ensure that these pipelines are simple and accessible. This aspect is especially important to ensure that all scientists, including those from LMICs, can have access, install and understand IARC's bioinformatics pipelines. Platforms, such as Docker, are used to ensure that the software required by our pipelines are directly available, making them easy to deploy and reproducible into a variety of different IT systems. The pipelines are developed around user-friendly software environments, such as Nextflow, that automatically orchestrate these different components together. Finally, the aim is to develop scalable and adaptable pipelines, ideally making them as applicable to smaller projects on personal computers (or the cloud) as they are applicable to large-scale projects undertaken on cutting edge high performance computer clusters.

More than 10 active developers generate a monthly average of 80 contributions to this project and more than 100 end-users outside IARC have "starred" our projects to express their support. Finally, IARC provides training opportunities in the use of these tools, including courses ranging from first time use of computational environments and user-friendly introductions to analysis tools, to advanced courses regarding the fine details in their application. Eight such courses have been organized in the past two years attended by a total of 88 early career and visiting scientists (ECVS) and 50 IARC staff. IARC bioinformaticians are also among the founding members of the recent "nf-core" (https://nf-co.re) initiative: an international collaboration with eight other research institutes to collect a curated set of bioinformatics analysis pipelines, avoiding duplicating efforts in each institute and distribute them wider to the community.

This project not only contributes to IARC's role in capacity building, but also assists genomic, transcriptomic, epigenomic, genetic and metabolomic projects within the Agency. As genomic data is increasingly used to assist tumour classification, for example malignant mesothelioma and lung neuroendocrine tumours, there is also a rising contribution from bioinformatics to projects in this area.

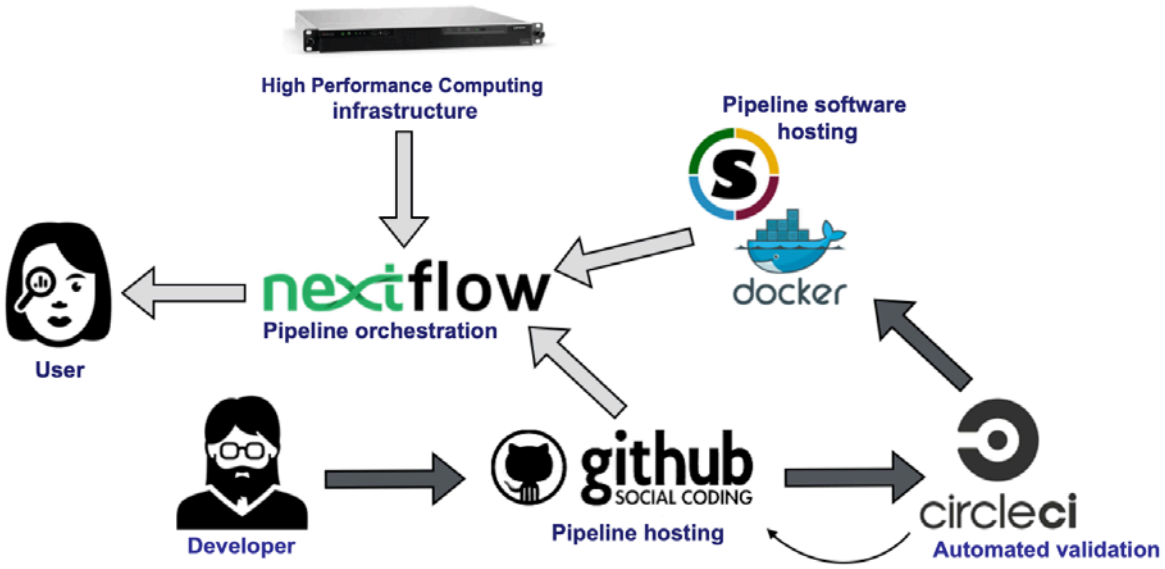


Figure – Framework of bioinformatics pipelines at IARC

Case Study #34: IARC POSTDOCTORAL PROGRAMME

MTS areas: These activities contribute to IARC MTS Project Tree objectives 4.1.1 and 5.3

- 4.1.1 Award fellowships and provide training through participation in collaborative research projects
- 5.3 Create and maintain key strategic partnerships with national, regional and international organisations

IARC Sections/Groups involved: led by the Education and Training Group (ETR) with contributions from all the IARC scientific Sections and Groups

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For more than five decades, the IARC Fellowship Programme has contributed to the development of human resources for cancer research and cancer control worldwide, a core statutory function of the Agency. The main goal is to provide training in cancer research in areas relevant to the Agency's programme. The Fellowship Programme also aims to catalyse the creation of collaborative links between IARC, cancer researchers, and research institutes around the world. Throughout its history, a specific focus of the IARC Fellowship Programme has been on training researchers from developing regions and since 2018 the programme has been restricted to applicants from LMICs. Fellowships are for a period of two years and are tenable at IARC. Fellows from LMICs can apply for a return grant, supporting the establishment of their research activity upon return to their home country after completion of their stay at IARC.

During the reporting period (January 2016 to end-June 2018) IARC Fellowships were awarded to 14 postdoctoral scientists, 10 coming from LMICs. As the outcome of a Fellowship awarded in a given year can only be documented at least one year after the end of the stay at IARC, data reported in this summary were therefore collected from Fellows awarded in previous years.

An online survey was carried out in 2015 and 2017, in order to document the outcomes and impact of the IARC Research Training and Fellowship Programme. A total of 42 former Fellows, covering a period from 2010 to 2017 completed the questionnaire. Results from both surveys were comparable and are summarized below.

Over two thirds of Fellows returned to their home country. The Fellows from LMICs who benefited from a return grant indicated that this helped their career as well as their institution through promotion, related funding, continuation of the project initiated at IARC, etc. (see example of a testimonial below).

At the time of the surveys, the vast majority of past Fellows were working in the public sector, and still active in cancer research. About one third of them were already managing their own group. The vast majority of Fellows continued to work with IARC at the end of their fellowship and an even greater number maintained international collaborations derived from their Fellowship (in addition to collaborations with IARC).

The vast majority of Fellows considered the Fellowship to be either decisive or helpful for their career. The areas of their fellowship training and experience that had the most impact on their

career were their collaborators (inside and outside of IARC), the scientific environment and the opportunities for international collaborations (see example of a testimonial below).

Although of small scale, the above reported results were consistent with data collected in 2012 and earlier, documenting outcomes of the IARC Fellowship Programme and demonstrating its success over decades in providing a fantastic opportunity for early career cancer researchers to assemble complementary skills in preparation for a high-level scientific career. Overall, more than 600 Fellows have benefited from the Fellowship Programme in more than 50 years. Many Fellows have become leading scientists in their field of cancer research (notably three of the six IARC Directors have been former IARC Postdoctoral Fellows), contributing to the production of evidence leading to the adoption of cancer prevention and control measures worldwide.

Examples of testimonials from IARC Fellows:

"*The return grant also provides us with an important platform and good reputation for our future studies. Following the return grant, we obtained further financial support from the Malaysian government to carry out further research on naso-pharyngeal carcinoma in the region*"

Dr Mohd. Arifin Kaderi
IARC Postdoctoral Fellow (2012) in the Genetic Cancer Susceptibility Group, now Assistant Professor, Department of Biomedical Science, International Islamic University Malaysia.

"*My experience at IARC brought me the necessary expertise to conduct cancer genomics studies and also allowed me to move to the next level in my career*"

Dr Felipe Vaca Paniagua
IARC Postdoctoral Fellow (2011) in the Molecular Mechanisms and Biomarkers Group, now Professor, National Autonomous University of Mexico, Iztacala Faculty, Mexico, Mexico.

To view more examples of testimonials from past of IARC Fellows see:
https://training.iarc.fr/fellowship-testimonials-3/

Case Study #35: THE 'NOUVEAU CENTRE' PROJECT

MTS areas: These activities contribute to IARC MTS Project Tree objectives 5.2, 5.3, 6.1.1 and 6.2

- 5.2 Oversee the strategic direction of the Agency and the implementation of its programme
- 5.3 Create and maintain key strategic partnerships with national, regional and international organisations
- 6.1.1 Provide sound management of human and infrastructure resources
- 6.2 Invest strategically towards increasing IARC's capacity

IARC Sections/Groups involved: led by the Section of Support to Research (SSR) with the Director's Office (DIR Office) Laboratory Services and Biobank (LSB) and Communications Group (COM)

The *Nouveau Centre* is a major building infrastructure project at the core of IARC's global research mission for the next 30–50 years. The new building is an integral part of IARC's business continuity plan, ensuring its continued presence in Lyon and the security of its physical infrastructure in the long term.

Lyon was officially confirmed as IARC's host city during the first meeting of the IARC Governing Council, in September 1965. Until May 1967, IARC was hosted by WHO in Geneva, before setting up its Lyon headquarters in offices at 16 avenue Maréchal Foch, in the sixth district of Lyon, in temporary premises made available by the mayor of Lyon at the time, Louis Pradel, who had strongly supported the hosting of IARC in his city.

In 1972, a new, purpose-built accommodation opened to host IARC's activities: the 14-floor tower building located at 150 cours Albert Thomas, in the eighth district of Lyon. Although it is an iconic building it is no longer well adapted to the needs of modern research and this, coupled with the ageing infrastructure and with the lack of capacity to expand, were the major drivers for a new building and the Nouveau Centre project.

The new IARC building will be located in the *Gerland Biodistrict* area of Lyon. The design and construction phase of the project is being managed by the *Métropole de Lyon* in cooperation with other French authorities. The project started in 2011, in close collaboration with local partners, and it is anticipated that IARC would be moving to its new premises in 2021. The *Nouveau Centre* is funded by the French government, the *Métropole de Lyon*, the *Région Auvergne-Rhône-Alpes*, and the *Ville de Lyon*.

The *Nouveau Centre* will offer IARC a building infrastructure that better suits modern research requirements, further enabling the efficient conduct and coordination of IARC's research, and promoting collaborations as a state of the art centre of excellence in the region. IARC will open its doors to the scientific community and the public, inter alia to host international as well as local meetings to promote IARC's values and share information on latest developments in cancer prevention.

The Nouveau Centre will underline IARC's leading role as the reference for international cancer research and will enable IARC to pursue its mission, to promote international collaboration in cancer research, while developing a leading biobank and ensuring the education and training of future cancer researchers, in adequate modern facilities.

Figure – Artist's impression of the approved project for the *Nouveau Centre*