International Agency for Research on Cancer

World Health Organization

Scientific Council **SC/54/6**
Fifty-fourth Session 18/12/2017

Lyon, 31 January–2 February 2018
Auditorium

PARALLEL SESSIONS

In order to engage as many Scientific Council members as possible in the discussions on cross-cutting research topics, the Director has decided to replace the plenary sessions by parallel sessions, followed by a short plenary session capturing the significant points. The following three topics will be discussed:

Topic	Page
Topic #1: Large-scale cohort studies, including the European Prospective Investigation into Cancer and Nutrition (EPIC) *Lead, Paul Brennan (GEP) and Support, Marc Gunter (NEP)* ➔ *Sasakawa Halls A&B*	2
Topic #2: Public cancer databases *Lead, Jiri Zavadil (MMB) and Support, James McKay (GCS) and Ian Cree (WCT)* ➔ *Princess Takamatsu Hall*	4
Topic #3: World Health Assembly Resolution on Cancer (May 2017) *Lead, Freddie Bray (CSU) and Support, Ed Seleiro (DIR Office)* ➔ *Auditorium*	7
IARC Organizational chart (Sections and Groups)	13

Topic #1: Large-scale cohort studies, including the European Prospective Investigation into Cancer and Nutrition (EPIC)

Lead, Paul Brennan (GEP) and Support, Marc Gunter (NEP) ➔ Sasakawa Halls A&B

There are opportunities to enhance the central EPIC database and biobank at IARC with data and biospecimens from the 23 collaborating centres. A discussion both about the priority research questions to be addressed and the future investment in this infrastructure will be valuable. In addition, IARC may have a role in leveraging collaboration across other cohorts (adult, adolescent and child) or consider supporting new cohorts in low- and middle-income countries (LMICs). The role IARC could play in such international activities will be explored in this discussion.

Background

Prospective cohort studies have been instrumental in evaluating the impact of a wide range of risk factors for cancer and other diseases, as well as for developing disease-prediction tools. Because they recruit study participants prior to disease onset and follow them throughout the life-course, prospective studies need to be of very large size, typically hundreds of thousands of participants, with adequate follow-up time to be able to study common diseases in a reliable manner. Among these, the EPIC cohort, including data and biospecimens from over 520 000 individuals from 23 centres, has been one of the most prominent.

The EPIC study has resulted in a large number of high profile papers, including those based solely on questionnaire data, those based on blood-based biomarkers for exposure, or even studies that attempt to identify blood-based biomarkers for early detection of cancer. It can be anticipated that with the increasing growth of blood-based proteomics, metabolomics and genomics technologies, these opportunities will increase substantially in the future. IARC has been instrumental in establishing other large-scale cohorts including the Russian adult cohort of over 150 000 participants, and the Golestan cohort of 50 000 adults in the North-east of Iran. Further, IARC scientists have established a large number of case-control studies in Africa, Latin America and Eastern Europe which could potentially lay the foundation for prospective cohort studies if the appropriate infrastructure and resources are available.

Given that IARC has been involved in the EPIC cohort since its onset, it is recognized as having a leadership role in the coordination and undertaking of large scale cohort studies, as well as consortia that aim to bring together large cohort studies from across the world. The most prominent is the NCI Cohort Consortium that aims to bring together representatives from all population based cohorts with at least 10 000 individuals with biological samples. Current membership includes cohorts with a combined total population of over 2.5 million individuals. Collaborative studies based within the Cohort Consortium involve large scale, ambitious, well-funded projects (usually through the NCI) and include some of the largest molecular epidemiology studies that have been conducted to date for breast, prostate, lung, colorectal, pancreatic and other cancers. Several of these are coordinated by IARC scientists (e.g. those on lung, kidney and HPV-related cancers) and IARC scientists also lead collaborative studies within the Consortium with a focus on specific exposures, for example, alcohol, diabetes, and hormonal factors across multiple cancer sites.

IARC has also played major roles in other transnational collaborative projects including the BBMRI-LPC consortium – a European Commission (EC) funded network of major biobanks across Europe. The BBMRI-LPC initiative laid the foundation for a 'European Cohort Consortium' comprising more than 20 European cohorts which, despite a major source of funding, has been held together under IARC's leadership and for which an application to fund the consortium through the EC will be submitted in 2018. Additional examples of consortia where IARC has played a leading role in their formation include the International Childhood Cancer Cohort Consortium (I4C) – an alliance of large-scale prospective cohort studies of children, that pools data and biospecimens from individual cohorts to study various modifiable and genetic factors in relation to childhood cancer risk, as well as the AGRICOH – an international consortium of agricultural cohort studies.

The last ten years have also seen the undertaking of a new wave of large cohort studies, the most prominent being the UK Biobank of 500 000 individuals with a policy of extensive phenotyping and open access to all data for scientists upon request. Similar cohorts are being planned or are underway in many other countries. These developments provide a number of opportunities as well as challenges for IARC scientists. Guidance in deciding an appropriate strategy over the medium term would be welcome.

Questions or areas of advice to be addressed by the SC members

1. What investments would most enhance the future value of EPIC, e.g. collection of more clinical data (recurrence, treatment) or new biospecimens (perhaps in a targeted fashion) in addition to the proposal to replenish the existing biobank (see Document SC/54/7)?
2. IARC has undertaken an important role in the coordination of cohort consortia, either within Europe (through the EC funded BBMRI-LPC programme) or globally (primarily through the NCI Cohort Consortium and the participation in consortia of birth cohorts). Is this an area where IARC senior scientists should continue to play a leading role, given that it will inevitably lead to a reduction in other areas of activity? What would be the priorities?
3. To what extent should IARC focus on the coordination and development of infant and mother-child cohorts, with a particular focus on childhood cancers? Should IARC consider developing a new cohort of teenagers/young adults with a long-term perspective of following them into later adulthood for cancer outcomes?
4. Are there particular 'omics' techniques or other tools (e.g. imaging) that are emerging and that are likely to have a major impact in exposure measurement or early detection within the next five years?
5. Are there particular cancers that IARC should focus on with respect to early detection studies? Should they be coordinated with large scale screening studies in order to identify high risk groups for screening?

Topic #2: Public cancer databases

Lead, Jiri Zavadil (MMB) and Support, James McKay (GCS) and Ian Cree (WCT)
➔ *Princess Takamatsu Hall*

An increasing wealth of scientific data is transforming our understanding of cancer, but these data are divided between many different databases and organizations. There are, nevertheless, increasing opportunities to access and conduct analyses on public cancer databases. IARC wishes to stimulate a discussion that may guide its future role in this area, and further promote its principal mission as a coordinator of international collaborative cancer research. An additional discussion is sought on the associated research opportunities and priorities for IARC drawing on such publicly available information.

Role of IARC in curating international databases

We wish to explore the possibility of an IARC-coordinated effort aiming to bring together cancer research institutions from the Participating States and the Agency's broader network of partners, to create a collaboration framework termed "International Collaboration for Cancer Classification and Research" (IC3R). The overarching goal of the IC3R is to foster and coordinate innovative cancer research opportunities using available genomic and other data, and to create new collaborative partnerships between its participants. The Agency, offering a unique international status, can serve as a trusted "broker" in the following areas: harmonization of cancer-related data generated by the IC3R participants, standard-setting and identification of critical gaps (e.g. non-uniform annotations, classifications, bioinformatics). Due to infrastructure constraints, IARC would not physically host the large data-sets, but it's scientific (including computational biology) and administrative expertise would allow it to coordinate access and exchange of data, such as from existing genome-scale data-sets (e.g. TCGA, PCAWG/ICGC consortia, see external partners) and data-sets that are yet to be generated (including by participating institutions outside these consortia).

IARC could provide secretariat for the IC3R framework, building on previous analogous and successful roles (Global Cancer Observatory, IARC Monographs, IARC Handbooks, IARC/WHO Blue Books, TP53 database, Exposome Explorer, Exposomics and the metabolome database HMDB 4.0). Forming closer partnerships and coordinating with established cancer genome consortia and standard-defining bodies will be critical for IC3R's success while data access could be mediated as public goods benefit to non-contributors (such as LMICs). Importantly, IC3R will provide the evidence to underpin the development of the next-generation tumour classification programme (ESC/WCT).

Examples of *proposed IC3R membership:* National Cancer Centres and cancer research institutions of the Participating States; analogous institutions from non-Participating States. *External partners:* PCAWG/International Cancer Genome Consortium (ICGC); The Cancer Genome Atlas (TCGA), The Global Alliance for Genomics and Health (GA4GH), Wellcome Trust Sanger Institute, Hinxton, Cambridge, UK; American Association for Cancer Research; others.

Opportunities for innovative research using cancer databases

Many key research activities at IARC rely on data from COSMIC, TCGA and ICGC data, and more recently on the Pan-Cancer Analysis of Whole Genomes (PCAWG) uniformly-analysed genome-scale datasets with user-friendly web tools for data exploration. In addition to the analysis of PCAWG/ICGC data, other activities such as Mendelian randomization approaches rely on the UK Biobank (GEP). Gene expression databases are used as part of genetic, epigenetic and etiology studies (GCS, EGE, MMB). IARC uses public cancer genomics data in various projects to query the tumour molecular landscapes, for hypothesis generation followed by testing in biological samples, in the areas of cancer genetic epidemiology (GEP) and susceptibility (GCS), epigenetics (EGE) and mutational signature studies (MMB, GEP, ICB). IARC activities such as the Grand Challenges project "Mutographs of Cancer" may generate hypotheses that can be further tested by the international consortia. We wish to discuss new approaches that IARC could take in analysing the publicly available data, what accompanying datasets could be furnished by the Agency and whether there are missed opportunities.

IARC Cancer Portal (ICP)

Different groups at IARC already maintain and/or develop public databases on different aspects of cancer, so we have considerable experience to draw on. The content and knowledge is specific to each database, reflecting the expertise of the database manager (TP53 mutations, incidence and mortality statistics, genetic variations, exposomics, metabolomics, etc.). These resources are popular and bring visibility to IARC's research. However, they are maintained independently, and use different platforms and annotation standards.

We propose the creation of a unified IARC Cancer Portal (ICP) for access to all IARC's public databases, with an IARC secretariat coordinating the participants' efforts. ICP will allow integrative searches through cross-referenced basic-level data underpinning tumour classification (Blue Books), cancer statistics (GCO), carcinogenic exposures (IMO classifications), genetic alterations (TP53 db), exposomics (Exposome Explorer), risk/protective factors (Handbooks/EPIC studies), IARC publications and ongoing projects. Searches in ICP will retrieve all publicly available data on a specific cancer type, using simple queries. Links to relevant outside public cancer databases could be incorporated, including ICD-O classifications, PCAWG/ICGC genome resources, relevant NCI databases, CDC's NPCR and SEER Incidence, NTP CEBS and Reports on Carcinogens and others. Better integration of IARC's own and public resources will facilitate access to users, improve the visibility of each individual resource and stimulate interactions between IARC groups, their collaborators, and cancer researchers worldwide.

Questions or areas of advice to be addressed by the SC members

1. Would IC3R fulfil an unmet need in the wider cancer research community; if so what might be the scope and which partner organizations should IARC seek out for further discussion?
2. Are there specific, novel research opportunities for IARC, with its unique mission, in relation to the ever growing number of public cancer databases?
3. Should IARC continue to invest in its current public databases and if so what would be the most effective approach?
4. Recognizing that any of these initiatives would require additional resources, does the Scientific Council have suggestions as to possible donors to approach for investment?

Topic #3: World Health Assembly Resolution on Cancer (May 2017)

Lead, Freddie Bray (CSU) and Support, Ed Seleiro (DIR Office) ➔ Auditorium

Introduction and rationale

According to WHO estimates, noncommunicable diseases (NCDs) were responsible for 56% of the 30.4 million global deaths at ages <70 in 2015, and one in three of these premature NCD deaths were due to cancer[1]. The disease ranks as the first or second cause of premature death in almost 100 countries worldwide, and, with ongoing transitions, is set to become the single most important cause of death and the leading barrier to increasing life expectancy in most countries in this century.

Such statistics have led to a global recognition of the need for high-level investment in the control of cancer alongside other major NCDs. In May 2017, governments from around the world adopted the World Health Assembly Resolution*, Cancer prevention and control in the context of an integrated approach* (WHA70.12[2]). The resolution builds on the *WHO Global Action Plan for the Prevention and Control of NCDs 2013–2020* (GAP[3]) and the UN Sustainable Development Goals 2030 (SDG[4]), including SDG 3.4 that targets a reduction of premature mortality from NCDs by one-third by 2030.

As stated in the Agency's *Medium-Term Strategy 2016–2020* (IARC MTS[5]), a defining feature of IARC is its position within the UN family and, more specifically, its unique place as the autonomous, specialized cancer agency of the World Health Organization (WHO). IARC staff worked with WHO colleagues to prepare the background report for the Resolution[6], ensuring the continuing impact of IARC's research on the development of global cancer policy through collaboration and strategic links with WHO.

The session aims to:

i) discuss the content of the resolution and the areas aligned with the IARC MTS,

ii) discuss the initiatives that IARC and WHO are jointly undertaking in response to the resolution, and

iii) identify other priority areas and opportunities for IARC, e.g. where further engagement in the response will significantly contribute to meeting the global targets of health and sustainable development over the next decade.

Key areas of the cancer resolution

The 2017 cancer resolution responds to the challenge of an increasing and inequitable cancer burden, providing countries with guidance on scaling up the implementation of integrated national cancer control plans. The approval of a specific resolution on cancer addresses some of the gaps left by the inclusion of cancer in the broader NCD agenda, for actions and policies specific to cancer prevention and control.

---

[1] http://www.who.int/gho/publications/world_health_statistics/2015/en/
[2] http://apps.who.int/gb/ebwha/pdf_files/WHA70/A70_R12-en.pdf
[3] http://apps.who.int/iris/bitstream/10665/94384/1/9789241506236_eng.pdf?ua=1
[4] https://sustainabledevelopment.un.org
[5] http://governance.iarc.fr/MTS/index.php
[6] http://apps.who.int/gb/ebwha/pdf_files/WHA70/A70_32-en.pdf

As well as invigorating WHO's mandate to deliver technical support to its Member States, the cancer resolution places renewed emphasis on IARC's strategy to provide the evidence-base for policy decisions on cancer control, including implementation research, requesting the WHO Director-General "*to collect, synthesize and disseminate evidence on the most cost-effective interventions"*. The resolution endorses the GAP, of which the updated (2017) Appendix 3[7] provides more detail with a list of 'best buys' and other recommended interventions for the prevention and control of NCDs, including cancer. Table 1 notes potential linkages between relevant areas of the resolution, the GAP, and the IARC MTS and specific activities of IARC Sections/Groups.

Cancer prevention and early detection are given prominence in the resolution, with an emphasis on tobacco control policies within the *WHO Framework Convention on Tobacco Control*, as well as affordable, feasible and cost-effective vaccine and screening programmes. Measuring the cancer burden to inform planning, through the development of population-based cancer registries, is also given central importance.

The resolution calls (page 5, paragraph 7) for the development by end-2019 of "*a public health- and policy-oriented world report on cancer [...] based on the latest available evidence and international experience, and covering the elements of this resolution, with the participation of all relevant parts of WHO, including IARC"*. This forthcoming *Global Report on Cancer* offers a unique opportunity for IARC and WHO to support WHO Member States in their effort to develop and implement evidence-based cancer control policies. The preparation of this Report has already started, coordinated by a joint WHO/IARC secretariat. This policy-oriented document will complement IARC's *World Cancer Report*, to be published in parallel, with a focus on cancer research for cancer prevention.

Questions or areas of advice to be addressed by the SC members

1. What should be the main priorities for the Agency's research programme in support of the WHO cancer resolution? Are there priority areas missing from the current MTS?
2. Given opportunities arising from the WHO cancer resolution, how should IARC liaise most effectively with WHO, other UN agencies and nongovernmental organizations?
3. How should IARC seek to support countries in implementing the resolution, e.g. IARC Participating States and WHO Member States?

---

[7] http://who.int/ncds/management/WHO_Appendix_BestBuys.pdf

Table 1. Specific areas covered in the WHO cancer resolution and linkages to IARC activities

Area	WHA70.12 resolution	Gap Appendix 3*	IARC MTS 2016–2020 – Project Tree Level 4 Objectives (Sections/Groups involved)
Surveillance	Page 3, para. 5: to collect high-quality population-based incidence and mortality data on cancer, for all age groups by cancer type, including measurements of inequalities, through population-based cancer registries, household surveys and other health information systems in order to guide policies and plans	OBJECTIVE 6 Policy options: • Strengthen human resources and institutional capacity for surveillance and monitoring and evaluation • Establish and/or strengthen a comprehensive NCD surveillance system, including reliable registration of deaths by cause, cancer registration, periodic data collection on risk factors and monitoring national response • Integrate NCD surveillance and monitoring into national health information systems	1.1.1 Expand the descriptive analyses of cancer incidence, mortality, prevalence and survival regionally and worldwide - Descriptive epidemiology of Cancer (CSU) 1.1.2 Improve the validity, range, timeliness and dissemination of appropriate cancer indicators available at the national, regional and global level - Global cancer indicators: development and dissemination (CSU) 1.2.1 Improve the availability, quality and dissemination of registry data, via IARC Regional Hubs and promote the role of population-based cancer registries in cancer control planning - Cancer registry support and development (CSU) 1.3.1 Publish WHO Classification of Tumours Series (WCT)

Area	WHA70.12 resolution	Gap Appendix 3*	IARC MTS 2016–2020 – Project Tree Level 4 Objectives (Sections/Groups involved)
Primary Prevention	Page 3, para. 6: to accelerate the implementation by States Parties of the WHO Framework Convention on Tobacco Control; and, for those Member States that have not yet done so, to consider acceding to the Convention at the earliest opportunity, given that the substantial reduction of tobacco use is an important contribution to the prevention and control of cancer Page 3, para. 7: to promote the primary prevention of cancers Page 3, para. 8: to promote increased access to cost-effective vaccinations to prevent infections associated with cancers, as part of national immunization schedules, based on country epidemiological profiles and health systems' capacities, and in line with the immunization targets of the global vaccine action plan	OBJECTIVE 3 Tobacco use: Overarching/enabling actions • Strengthen the effective implementation of the WHO FCTC and its protocols • Establish and operationalize national mechanisms for coordination of the WHO FCTC implementation as part of national strategy with specific mandate, responsibilities and resources For member states that are not parties to the WHO FCTC: • Consider implementing the measures set out in the WHO FCTC and its protocols, as the foundational instrument in global tobacco control OBJECTIVE 4 Policy options: • Train the health workforce and strengthen the capacity of health systems, particularly at the primary care level, to address the prevention and control of noncommunicable diseases Best buys: • Vaccination against human papillomavirus (2 doses) of 9–13 year old girls Other: • Prevention of liver cancer through hepatitis B immunization	3.1.1 Analyse the efficacy of primary cancer prevention strategies - Implementation and monitoring of human papilloma virus (HPV) vaccination and HPV-based screening in LMICs (ICE) - Epidemiology and prevention of gastric cancer (PRI) - Gambia Hepatitis Intervention Study (GHIS) 3.2.1 Identify factors influencing the effective implementation of primary and secondary prevention programmes - Expansion and evaluation of Cancer Prevention Recommendations (ENV) - Implementation studies of HPV vaccination (PRI) - Evaluation of cervical cancer control measures in developing countries (SCR) 3.3.1 Publish IARC Handbooks on Cancer Prevention - IARC Handbooks on Cancer Prevention (IHB)

Area	**WHA70.12 resolution**	**Gap Appendix 3***	**IARC MTS 2016–2020 – Project Tree Level 4 Objectives (Sections/Groups involved)**
Early detection and treatment	Page 3, para. 9: to develop, implement and monitor programmes, based on national epidemiological profiles, for the early diagnosis of common cancers, and for screening of cancers, according to assessed feasibility and cost-effectiveness of screening, and with adequate capacity to avoid delays in diagnosis and treatment	OBJECTIVE 4 Policy options: • Scale up early detection and coverage, prioritizing very cost-effective high-impact interventions including cost-effective interventions to address behavioural risk factors • Train the health workforce and strengthen the capacity of health systems, particularly at the primary care level, to address the prevention and control of noncommunicable diseases Best buys: • Prevention of cervical cancer by screening women aged 30–49 years, either through: visual inspection with acetic acid (VIA), Pap smear every 3–5 years; HPV test every 5 years Effective: • Screening [of breast cancer] with mammography (once every 2 years for women aged 50–69 years) Other: • Oral cancer screening in high-risk groups • Population-based colorectal cancer screening, including through FOBT, as appropriate, at ages >50 years	3.1.2 Analyse the efficacy of secondary cancer prevention strategies - Implementation and monitoring of HPV vaccination and HPV-based screening in LMICs (ICE) - Cervical cancer screening strategies for LMICs (PRI) 3.2.1 Identify factors influencing the effective implementation of primary and secondary prevention programmes - Evaluation of cervical cancer control measures in developing countries (SCR) - Evaluation of colorectal and oral cancer screening (SCR) - Cancer Screening Initiatives and their Impact in Five Continents (SCR) 3.3.1 Publish IARC Handbooks on Cancer Prevention - IARC Handbooks on Cancer Prevention (IHB)

Area	WHA70.12 resolution	Gap Appendix 3*	IARC MTS 2016–2020 – Project Tree Level 4 Objectives (Sections/Groups involved)
Research – including implementation, health outcomes and cost-effectiveness	Page 4, para. 14: to promote cancer research to improve the evidence base for cancer prevention and control, including research on health outcomes, quality of life and cost-effectiveness Page 5, para. 2: to collect, synthesize and disseminate evidence on the most cost-effective interventions for all age groups, and support Member States in the implementation of these interventions; and to make an investment case for cancer prevention and control Page 5, para. 7: to develop, before the end of 2019, the first periodic public health- and policy-oriented world report on cancer, in the context of an integrated approach, based on the latest available evidence and international experience, and covering the elements of this resolution, with the participation of all relevant parts of WHO, including IARC, and in collaboration with all other relevant stakeholders, including cancer survivors Page5, para. 8: to enhance the coordination between IARC and other parts of WHO on assessments of hazards and risks, and on the communication of those assessments	OBJECTIVE 5 Policy options: • Develop and implement a prioritized national research agenda for NCDs • Prioritize budgetary allocation for research on NCD prevention and control • Strengthen human resources and institutional capacity for research • Strengthen research capacity through cooperation with foreign and domestic research institutes	3.1.3 Enhance understanding of the factors affecting cancer prognosis - Improving the quality of breast cancer screening, early diagnosis and treatment services in LMICs (SCR) - Study lifestyle and environmental determinants of cancer risks, prognosis and cancer outcomes (ENV) 3.2.1 Identify factors influencing the effective implementation of primary and secondary prevention programmes - Expansion and evaluation of Cancer Prevention Recommendations (ENV) - Implementation studies of HPV vaccination (PRI) - Evaluation of cervical cancer control measures in developing countries (SCR) - Evaluation of colorectal and oral cancer screening (SCR) - Cancer Screening Initiatives and their Impact in Five Continents (SCR)

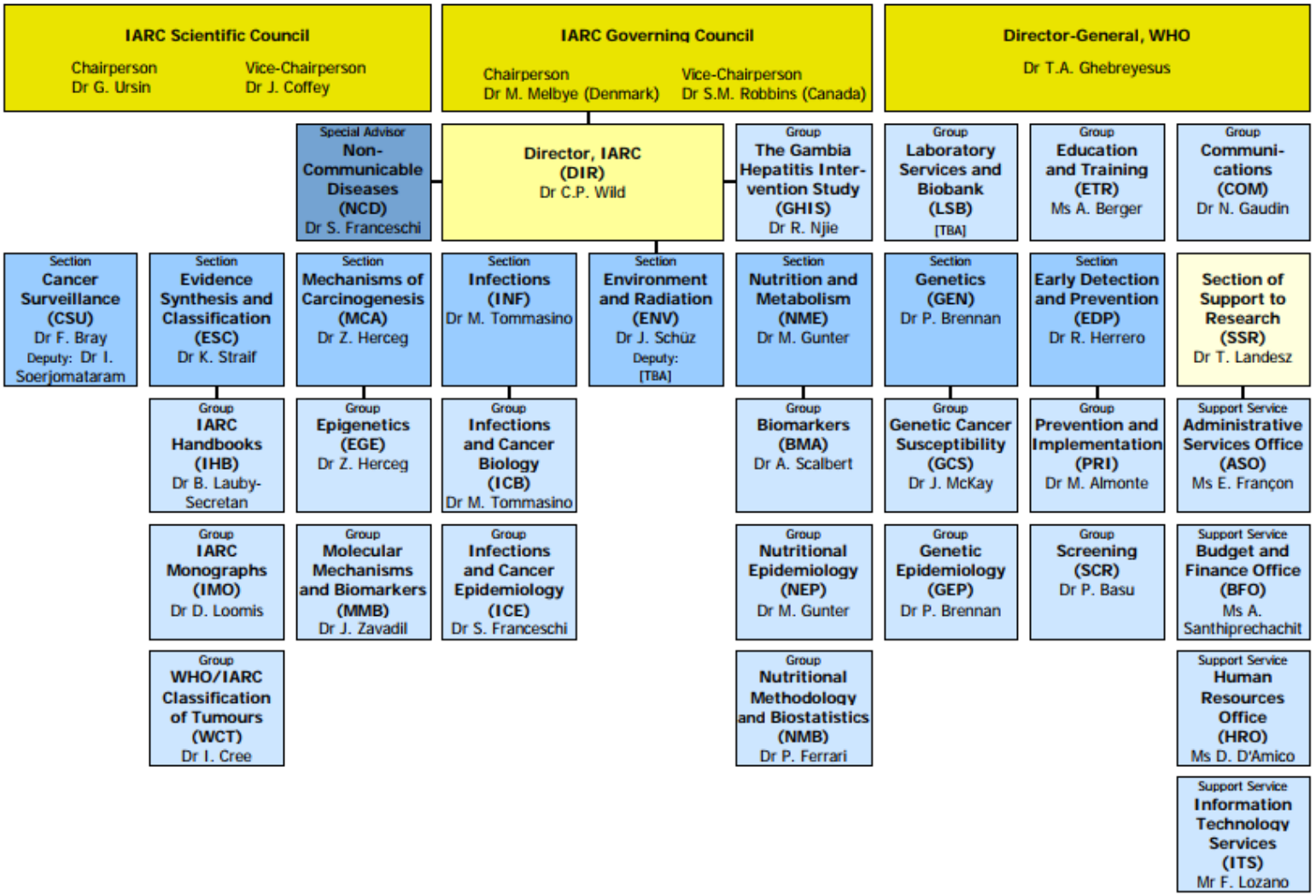
* '*Best buys*': Effective interventions with cost effectiveness analysis ≤ 100 I$ per DALY averted in LMICs.
Effective: interventions with cost effectiveness analysis > 100 I$ per DALY averted in LMICs.
Other: recommended interventions from WHO guidance (cost effective analysis not available).

Specific objectives mentioned in the GAP Appendix 3:
OBJECTIVE 3 - Reducing modifiable risk factors for NCDs and underlying social determinants through creation of health-promoting environments
OBJECTIVE 4 - Strengthen and orient health systems to address the prevention and control of NCDs and the underlying social determinants through people-centered primary health care and universal health coverage
OBJECTIVE 5 - To promote and support national capacity for high-quality research and development for the prevention and control of NCDs
OBJECTIVE 6 - To monitor the trends and determinants of NCDs and evaluate progress in their prevention and control

IARC Organizational Chart (see below and here)

International Agency for Research on Cancer
World Health Organization

1 November 2017



/mg