About UICC

The Union for International Cancer Control (UICC) is the leading international non-governmental organization dedicated to global cancer control.

Founded in 1933, UICC unites over 300 member organizations, specialized and engaged in cancer control, in more than 100 countries across the world.

UICC’s mission is to **connect, mobilize and support** organizations, leading experts, key stakeholders and volunteers in a dynamic community working together to eliminate cancer as a life-threatening disease for future generations.

UICC works closely with its member organizations and partners to implement a comprehensive strategy that includes:

- promoting the World Cancer Declaration
- organizing the World Cancer Congress
- raising awareness through the World Cancer Campaign
- coordinating World Cancer Day annually, on 4 February
- reviewing and disseminating the TNM (tumour-node-metastasis) classification of malignant tumours
- developing effective cancer control programmes especially in low- and middle-income countries
- changing cancer-related beliefs and behaviour through information and education
- creating special initiatives in prevention, early detection, access to treatment and supportive care
- awarding international cancer fellowships
- producing cutting-edge scientific publications, such as the *International Journal of Cancer*

UICC is governed by its member organizations, which meet in a general assembly, held in conjunction with the World Cancer Congress, every two years. Between assemblies, a board of 17 directors, elected by the general assembly, acts as the executive body of the UICC.

UICC works closely with the World Health Organization (WHO), the International Agency for Research on Cancer (IARC), and the Programme of Action for Cancer Therapy (PACT) and has consultative status with the UN Economic and Social Council. It offers corporate partners a unique opportunity to demonstrate social responsibility on a global scale. Every two years.

UICC is non-profit, non-political and non-sectarian. Its headquarters are in Geneva, Switzerland. www.uicc.org
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993 DNA methylation testing with S5 for triage of high-risk HPV positive women
Rachael Adcock, Belinda Nedjai, Attila T. Lorincz, Dorota Scibior-Bentkowska, Rawinder Banwait, Norah Torrez-Martinez, Michael Robertson, Jack Cuzick, Cosette M. Wheeler, and On behalf of the NewMexico HPV Pap Registry Steering Committee

Human papillomavirus (HPV) testing is a more sensitive but less specific approach for cervical cancer screening than cytology. Methylation testing of host and viral genes has emerged as a promising approach for the triage of women with high-risk HPV. In this population-based study, using the DNA methylation S5 classifier as a triage test for high-risk HPV-positive women yields significantly greater sensitivity and similar positive predictive values for CIN3+ detection than HPV genotyping or cytology triage. Furthermore, S5 can improve discrimination between low- and high-grade cervical precancer, providing valuable information in the often complex and uncertain diagnosis of CIN2.

1005 Meat consumption and risk of esophageal and gastric cancer in the Golestan Cohort Study, Iran
Giulia Collatuzzo, Arash Etemadi, Masoud Sotoudeh, Arash Nikmanesh, Hossein Poustchi, Masoud Khoshnia, Akram Pourshams, Maryam Hashemian, Gholamreza Roshandel, Sanford M. Dawsey, Christian C. Abnet, Farin Kamangar, Paul Brennan, Paolo Boffetta, and Reza Malekzadeh

While high intakes of red meat and processed meat are risk factors for certain cancer types, especially colorectal cancer, associations with esophageal cancer (EC) and gastric cancer (GC) remain uncertain. Here, meat intake and EC and GC risk were examined in a population in northeast Iran with overall low meat intake, except for high consumption of organ and chicken meat. Hazards regression modeling reveals associations between red meat intake and elevated GC risk, particularly non-cardia GC. There was no association with EC or its subtypes. Further study is needed to determine possible etiological involvement of red meat in GC development.

1013 Infant feeding practices and childhood acute leukemia: Findings from the Childhood Cancer & Leukemia International Consortium
Jeremy M. Schraw, Helen D. Bailey, Audrey Bonaventure, Ana M. Mora, Eve Roman, Beth A. Mueller, Jacqueline Clavel, Eleon T. Petridou, Maria Karalexi, Evangelia Ntzani, Sameera Ezzat, Wafaa M. Rashed, Erin L. Marcotte, Logan G. Spector, Catherine Metayer, Alice Y. Kang, Corrado Magnani, Lucia Miligi, John D. Dockerty, Juan Manuel Mejía-Aranguré, Juan Carlos Nuñez-Enriquez, Claire Infante-Rivard, Elizabeth Milne, and Michael E. Scheuerer

Breastfeeding may protect against childhood acute lymphoblastic and acute myeloid leukemia (ALL/AML), but few studies have examined exclusive breastfeeding or interactions with other early life exposures. In this international pooled analysis, breastfeeding was associated with reduced risk of ALL/AML. Risk of ALL was lowest among exclusively-breasted children or breastfed children who also attended day care. The results indicate a dose-response relationship between breastfeeding and leukemia and highlight the potentially complex joint effects of early life exposures. Few risk factors for ALL and AML have been identified, and the findings support the need to promote breastfeeding for leukemia prevention.
1024 Risk of secondary nonhematologic malignancies after allogeneic stem cell transplantation: A nationwide case-control cohort study
Sung-Soo Park, Si-Hyun Park, and Seunghoon Han
While patients who received allogeneic hematopoietic stem cell transplantation (allo-SCT) are at increased risk of secondary nonhematological malignancies, the development of standardized screening strategies is hindered by regional and ethnic differences affecting cancer incidence and site. In this large nationwide, retrospective cohort study in Korea, the 10-year cumulative incidence of secondary nonhematological malignancies in allo-SCT was 4.23%, compared to the general population, the risk was higher for head, neck and esophagus cancers, upper gastrointestinal tract cancers, colorectal cancer, thyroid cancer and gynecological cancers following allo-SCT, suggesting the need to establish robust specific screening programs.

1033 Circulating free testosterone and risk of aggressive prostate cancer: Prospective and Mendelian randomisation analyses in international consortia
Eleanor L. Watts, Aurora Perez-Cornago, Georgina K. Fensom, Karl Smith-Byrne, Urwah Noor, Colm D. Andrews, Marc J. Gunter, Michael V. Holmes, Richard M. Martin, Konstantinos K. Tsilidis, Demetrios Albanes, Aurelio Barrientes, Bas Bueno-de-Mesquita, Chu Chen, Barbara A. Cohn, Niki L. Dimou, Luigi Ferrucci, Leon Flicker, Neal D. Freedman, Graham G. Giles, Edward L. Giovannucci, Gary E. Goodman, Christopher A. Haiman, Graeme J. Hankey, Jiaqi Huang, Wen-Yi Huang, Lauren M. Hurwitiz, Rudolf Kaaks, Paul Knekt, Tatsuhiko Kubo, Hilde Langseth, Gail Laughlin, Loic Le Marchand, Tapio Luostarinen, Robert J. Maclnnis, Hanna Q. Mäenpää, Satu Mäenpää, E. Jeffrey Metter, Kazuya Mikami, Lorelei A. Mucci, Anja W. Olsen, Kotaro Ozasa, Domenico Palli, Kathryn L. Penney, Elizabeth A. Platz, Harri Rissanen, Norie Sawada, Jeannette M. Schenk, Pär Stattin, Akiko Tamakoshi, Elin Thysell, Chiaojung Jillian Tsai, Shoichiro Tsugane, Lars Vatten, Elisabete Weiderpass, Stephanie J. Weinstein, Lynne R. Wilkens, Bu B. Yeap, The PRACTICAL Consortium, CRUK, BPC3, CAPS, PEGASUS, Naomi E. Allen, Timothy J. Key, and Ruth C. Travis
The Endogenous Hormones, Nutritional Biomarkers and Prostate Cancer Collaborative Group (EHNBPCCG) is a pooled dataset of prospective studies of prostate cancer risk. Using this data, the authors conducted blood-based analysis and Mendelian randomisation analysis to determine the association between circulating testosterone and overall risk of prostate cancer, as well as looking at risk of aggressive disease and early-onset cancer separately. They found strong evidence that higher concentrations of circulating testosterone increases the risk of prostate cancer, including aggressive subtypes. This is the largest collection of prospective blood-based observational and genetic data on sex hormones and prostate cancer risk to date.

1047 Performance of HPV E6/E7 mRNA assay as primary screening test: Results from the NTCC2 trial
Paolo Giorgi Rossi, Guglielmo Ronco, Pamela Mancuso, Francesca Carozzi, Elena Allia, Simonetta Bisani, Anna Gillio-Tos, Laura De Marco, Raffaella Rizzolo, Daniela Gustinucci, Annarosa Del Mistro, Helena Frayle, Massimo Confortini, Anna Iossa, Elena Cesarini, Simonetta Bulletti, Basilio Passamonti, Silvia Gori, Laura Toniolo, Alessandra Barca, Laura Bonvicini, Francesco Venturelli, Maria Benevolo, and NTCC2 Working Group
Human papillomavirus (HPV) DNA-based assays are now widely recommended for cervical cancer screening, but they lack specificity. As a primary screening test, E6/E7 mRNA testing has shown a similar sensitivity for CIN3+ but a lower positivity rate than HPV DNA testing. This trial study shows that primary E6/E7 mRNA screening would miss about 3% of CIN3+ cases. Overall positivity would be 22% lower than that of HPV DNA. Triage with cytology or p16/ki67 dual staining would only marginally decrease overall colposcopy referral if retesting of E6/E7 mRNA-positive/triage-negative women was performed with HPV DNA assays after 12 months.
Inflammatory myofibroblastic tumor: A multi-institutional study from the Pediatric Surgical Oncology Research Collaborative

Barrie S. Rich, Joanna Fishbein, Timothy Lautz, Nathan S. Rubalcava, Tanvi Kartal, Erika Newman, Pei En Wok, Rodrigo L. P. Romao, Richard Whitlock, Bindi Naik-Mathuria, Stephanie F. Polites, Katrine Løfberg, Danny Lascano, Eugene Kim, Jacob Davidson, Andrena Büttler, Zachary J. Kastenberg, Scott S. Short, Rebecka L. Meyers, Rosemarie Mastropolo, Marcus M. Malek, Jennine Weller, Ahmer Irfan, Daniel S. Rhee, Alan F. Utria, David H. Rothstein, Kimberly Riehle, Sarah Jane Commander, Elisabeth Tracy, Kerri Becktell, Brian Hallis, Dave Lal, Orville Li, Dorothé B. Dal-Soglio, Nelson Piché, Oswaldo Gomez Quevedo, Andrew J. Murphy, Andrew M. Davidoff, Jo Cooke Barber, Erin Watters, Roshni Dasgupta, and Richard D. Glick

Inflammatory myofibroblastic tumor (IMT) is a heterogeneous malignancy with variable patterns of histology and behavior that primarily affects children and young adults. Owing to its rarity, however, IMT remains poorly understood. Here, data from a multi-institutional retrospective review of children and young adults with IMT was assessed to identify novel characteristics and thereby advance understanding of IMT. Analyses reveal a 5-year recurrence rate of 20%, wherein respiratory symptoms, tumor size and metastatic disease were linked to recurrence. Moreover, positive surgical margins did not correlate with event-free survival, calling into question the role of aggressive surgical resection in IMT.

Sleep duration and risk of cancer incidence and mortality: A pooled analysis of six population-based cohorts in Japan

Calistus Wilunda, Sarah Krull Abe, Thomas Svensson, Norie Sawada, Shoichiro Tsugane, Keiko Wada, Chisato Nagata, Takashi Kimura, Akiko Tamakoshi, Yumi Sugawara, Ichiro Tsuji, Hidemi Ito, Tetsuya Kitamura, Ritsu Sakata, Tetsuya Mizoue, Keitaro Matsuo, Keitaro Tanaka, Yingsong Lin, Manami Inoue, and For the Research Group for the Development and Evaluation of Cancer Prevention Strategies in Japan

Habitual sleep is a critical determinant of health and a potential indicator of cancer outcome. The relationship between sleep duration and cancer morbidity and mortality, however, remains unclear. In this assessment of data from the Japan Cohort Consortium, the authors show that excess sleep is associated with increased cancer mortality in both men and women, as well as with elevated cancer incidence specifically in women. Among postmenopausal women, both long and short sleep durations were linked to increased cancer mortality. The findings indicate that sleep duration is an important variable in cancer, with implications for cancer prevention.

Detection of circulating tumor human papillomavirus DNA before diagnosis of HPV-positive head and neck cancer

Eleni M. Rettig, Daniel L. Faden, Shaiba Sandhu, Kristine Wong, William C. Faquin, Chloe Warinner, Phil Stephens, Sunil Kumar, Charlotte Kuperwasser, Jeremy D. Richmond, Ravindra Uppaluri, Mark Varvaress, Rosh Sethi, Glenn J. Hanna, and Herve Sroussi

Circulating tumor human papillomavirus (HPV) DNA (ctHPVDNA) is associated with tumor burden and response to treatment in HPV-positive head and neck squamous cell carcinoma (HNSCC). In this case-control study, ctHPVDNA was detected in plasma greater than 3 years prior to diagnosis of HPV-positive HNSCC. This is the first study to demonstrate that ctHPVDNA is detectable prior to clinical development of an HPV-positive cancer and thus, may allow for earlier diagnosis of HPV-positive HNSCC.
Somatic genomic landscape of East Asian epithelial ovarian carcinoma and its clinical implications from prospective clinical sequencing: A Korean Gynecologic Oncology Group study (KGOG 3047)
Jason K. Sa, Jihye Kim, Sokbom Kang, Sang Wun Kim, Taejong Song, Seung-Hyuk Shim, Min Chul Choi, Jae Hong No, Jae-Yun Song, Deokhoon Kim, Yong-Man Kim, Jae-Hoon Kim, and Jeong-Won Lee
Epithelial ovarian carcinoma has a high mortality rate, and as a heterogeneous disease, it can be difficult to treat. Here, the authors profiled the genetic characteristics of ovarian carcinomas among 652 patients in Korean hospitals. By sequencing the tumors, they determined that more than 80% of the cancers contained at least one actionable genetic alteration, most commonly in the genes TP53, BRCA1, BRCA2 or MYC. Machine-learning-based algorithms also uncovered correlations between certain molecular markers and response to platinum-based treatment and the PARP inhibitor olaparib. These results suggest that clinical sequencing could improve personalized treatment of ovarian carcinoma.

CANTO-RT: Skin toxicities evaluation of a multicentre large prospective cohort of irradiated patients for early-stage breast cancer
Sofiane Allali, Matthieu Carton, Thomas Sarrade, Ophélie Querel, Alexandra Jacquet, Sofia Rivera, Youssef Ghannam, Karine Peignaux, Philippe Guibert, Claire Chara-Brunaud, Julien Blanchecotte, David Pasquier, Séverine Racadot, Céline Bourgier, Alain Labib, Julien Geffrelot, Ahmed Benyoucef, François Paris, Paul Cottu, Fabrice André, and Youlia Kirova
Cutaneous toxicities are a significant concern in the treatment of early-stage breast cancer. To minimise their occurrence, however, a greater understanding of factors influencing their development is needed. Here, using data from the prospective, multicentre CANTO study, occurrence of cutaneous toxicities was found to be influenced constantly over time by obesity and type of surgery received by patients, with both obesity and surgery acting as independent risk factors. Radiotherapy technique further impacted the occurrence of cutaneous toxicities. The results indicate that the modification of breast cancer treatment according to patient characteristics is a promising strategy for minimising cutaneous toxicities.

Association between medical androgen deprivation therapy and long-term cardiovascular disease and all-cause mortality in nonmetastatic prostate cancer
Rachel B. Forster, Anders Engeland, Rune Kvåle, Vidar Hjellvik, and Tone Bjørge
Existing evidence suggests that prostate cancer patients receiving androgen deprivation therapy are at increased risk of cardiovascular disease. The relationship between prostate cancer treatment and cardiovascular disease remains unclear, however. Using longitudinal registry data for all prostate cancer patients in Norway, our study identifies an increased risk of cardiovascular disease and mortality in patients treated with androgen deprivation therapy. The increased risk is most pronounced in patients with low or moderate prior risk of cardiovascular disease and longer duration of treatment. The findings contribute new evidence to the ongoing discussion about the use of hormonal therapy.

Evaluation of effectiveness, acceptability and safety of thermal ablation in the treatment of cervical neoplasia in Burundi
Catherine Sauvaget, Sylvestre Bazikamwe, Eric Lucas, Athanase Ndayikengurukiye, Salvador Harerimana, and Prebo Barango
Cervical cancer remains a major public health issue in resource-constrained settings. Appropriate management of precancer lesions is a key strategy to achieve cervical cancer elimination. Many low-income countries provide cryotherapy as an ablative treatment, but thermal ablation may be a more practical and sustainable alternative. This longitudinal study reports the efficacy of thermal ablation in the treatment of cervical neoplasia in Burundi. Thermal ablation had a high cure rate at 12 months and was found to be safe and acceptable, supporting its potential use at the primary health care level in a ‘screen-and-treat’ approach.
Infectious Causes of Cancer

Systematic analysis of Kaposi’s sarcoma (KS)-associated herpesvirus genomes from a KS case-control study in Cameroon: Evidence of dual infections but no association between viral sequence variation and KS risk

Vickie A. Marshall, Nicholas C. Fisher, Charles A. Goodman, Elena M. Cornejo Castro, Isabella Liu, Sirish Khanal, Benjamin M. Holdridge, Abigail L. Thorpe, Nazzarena Labo, Kristen B. Stolka, Jennifer J. Hemingway-Foday, Mahamat Abassora, Paul N’Dom, Jennifer S. Smith, Neneh Sallah, Anne L. Palser, Paul Kellam, Brandon F. Keele, and Denise Whitby

Kaposi sarcoma-associated herpesvirus (KSHV), the cause of Kaposi sarcoma (KS), is classified into different subtypes based on genetic variation. Little is known, however, about whether variations in KSHV genomes differ among KS patients in the same geographic region. Here, no link was found between viral sequence variations and KS risk, based on comparison of KSHV genomes from KS patients in the same population. Several participants exhibited evidence of at least two divergent KSHV genomes, indicating dual infection with distinct KSHV subtypes. The observation of highly recombinant KSHV sequences and KSHV coinfection contributes to improved understanding of KSHV epidemiology.

Innovative Tools and Methods

Redesign of a rapid, low-cost HPV typing assay to support risk-based cervical screening and management

Kanan T. Desai, Clement A. Adepliti, Mark Schiffman, Didem Egemen, Julia C. Gage, Nicolas Wentzensen, Silvia de Sanjose, Robert D. Burk, and Kayode O. Ajenifuja

Due to cost and perceived complexity, most existing human papillomavirus (HPV) assays for cervical cancer screening are designed to yield a pooled result for the carcinogenic HPV types. Here, to promote rapid, affordable and risk-based cervical screening, an existing isothermal DNA amplification test was redesigned to group the carcinogenic HPV types into four channels based on clinical importance (HPV16; HPV18/45; HPV 31/33/35/52/58 and HPV 39/51/56/59/68). In masked retesting of 453 Nigerian specimens, the new ScreenFire assay showed good-to-excellent type group agreement with prior PCR testing. When validated, the redesigned test could support risk-based screening in resource-limited settings.

Molecular Cancer Biology

Amplified Ca\(^{2+}\) dynamics and accelerated cell proliferation in breast cancer tissue during purinergic stimulation

Mikkel B. Henningsen, Kezia McWhan, Vibeke S. Dam, Marco Mele, Katrine R. Hauerslev, Ninna C. S. Voss, Parag D. Dabir, Eva Balling, Helene L. Pedersen, Pernille Vahl, Tonje Johansen, Trine Tramm, Peer M. Christiansen, and Ebbe Boedtkjer

Molecular mechanisms influencing intracellular Ca\(^{2+}\) dynamics are deregulated in cancer cell lines. However, many implications of deregulated Ca\(^{2+}\) signaling during carcinogenesis remain unclear. Using fresh human and murine tissue biopsies, here the authors show that resting intracellular Ca\(^{2+}\) levels, organellar Ca\(^{2+}\) storage and intracellular Ca\(^{2+}\) responses to nucleotides and cholinergic stimuli are elevated during breast, but not colon, carcinogenesis. Nucleotides stimulate proliferation in breast cancer tissue within the elevated nucleotide concentration range observed in the tumor microenvironment, whereas cell death is induced only at higher concentrations. The authors propose that amplified Ca\(^{2+}\) signals facilitate breast malignancy.

Tumor Markers and Signatures

Predictive value of chromosome 18q11.2-q12.1 loss for benefit from bevacizumab in metastatic colorectal cancer: A post hoc analysis of the randomized phase III-trial AGITG-MAX

Erik van Dijk, Erik van Werkhoven, Rebecca Asher, Jennifer K. Mool, David Espinoza, Hendrik F. van Essen, Harm van Tinteren, Nicole C. T. van Grieken, Cornelis J. A. Punt, Niall C. Tebbutt, and Bauke Ylstra

Survival among metastatic colorectal cancer (mCRC) patients can be significantly improved with the monoclonal antibody bevacizumab, though patient selection is needed in order to ensure favorable cost-benefit ratio. A promising marker for this task is chromosome 18q11.2-q12.1 loss. Here, the predictive capacity of 18q loss was evaluated in mCRC samples from bevacizumab-treated patients enrolled in the AGITG-MAX randomized trial. Data show that, compared to patients without 18q loss, those lacking 18q had better progression-free survival following bevacizumab therapy. The study highlights the utility of 18q as a predictive marker for bevacizumab response and cost-benefit assessment in mCRC patients.
Diagnostic potential of nanoparticle aided assays for MUC16 and MUC1 glycovariants in ovarian cancer

Shruti Jain, Nimrah Nadeem, Benjamin Ulfenborg, Maria Mäkelä, Shamima Afrin Ruma, Joonas Terävä, Kaisa Huhtinen, Janne Leivo, Björg Kristjansdottir, Kim Pettersson, Karin Sundfeldt, and Kamlesh Gidwani

While MUC16 represents a promising serum marker for epithelial ovarian cancer, its inadequate specificity has impeded clinical applications. Our study using a novel immunoassay with fluorescent nanoparticles coated with glycan structure-specific binders shows that cancerous sub-forms of MUC16 and MUC1 can be quantitated while suppressing mucin signals from confounding benign conditions. In ovarian cyst fluids, immunoassays for MUC16 and MUC1 STn glycovariants were superior to conventional CA125 and CA15-3 immunoassays. In paired serum samples, the main benefits were seen in postmenopausal and early-stage patients. The results pave the way for improved routine differential diagnostics of epithelial ovarian cancer.

Erratum

The "What’s new?” texts are edited by professional science writers, and approved by the authors.

Cover legend: KSHV splits network of near full-length genomes with K1 / K15 subtypes indicated by color. Whole-genome splits network of 40 study and 16 published sequences created using SplitsTree v4.15.1. A total of approximately 130,000 positions were included in the final data set with bootstrap values over 80 reported. Repetitive sequence regions were removed from the analysis. The analysis indicates KSHV genomes are highly recombinant. The KSHV full and partial genomes used for phylogenetic analyses included: GK18 (NC_009333), BC-1 (U75698.1), Japan/Miyako sequences (LC200587.1-LC200589.1), BCBL-1 (HQ404500.1), JSC-1 (MK143395.1), KSHV-BAC36 (HQ404500.1), BrK.219 (KFS88566.1), BCBL-1 (MT936340.1), Zambian sequences ZM007-ZM130 (KT271453-KT271468), and newly published current study sequences from Cameroon (OL829860-OL829899). See the related article by Marshall et al., pages 1127-1141.