WORLD OBESITY

World Cancer Research Fund International

# HOT TOPIC CONFERENCE:

## Obesity, Physical Activity & Cancer:

## Life course influences and mechanisms

WORLD OBESITY

World Cancer Research Fund International

## Dear Colleague

We are delighted to welcome you to London for this conference jointly organised by World Cancer Research Fund International and World Obesity Federation. This is a follow-up to the highly successful first OPAC conference we organised together in 2013, and we're confident you will find this year's programme equally inspiring and informative.

This year's topics include several sessions on the mechanisms underpinning the links between obesity and physical activity, and cancer risk and survival. Other sessions look at how early life events are linked to obesity and cancer susceptibility in later life as well as best practice for turning scientific findings into effective policy actions. Future research needs will be shared and discussed throughout.

We know how useful it is for scientific, health and policy professionals working in these areas to come together to share latest findings and take advantage of the excellent networking and collaborative opportunities. We encourage you to take part in the audience and panel discussions, which are always such a prominent feature of this conference.

On behalf of both our organisations we would like to thank all our invited speakers and hope that you enjoy the conference and are also able to enjoy some time in London while you are here.

With best wishes.

World Obesity Federation & World Cancer Research Fund International

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## Useful Information

SCOPE Accredited

CPD CERTIFIED The CPD Certification Service

### Wi-Fi Details

Login: CDH
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### Professional Development

Attendance Provides 4 SCOPE points and 16 CPD points

### Social Media

Include the official event hashtag, #OPAC2 in all social media posts.

Tweet using this hashtag and tag World Obesity and WCRF International:

@WorldObesity
@wcrfint

# HOST ORGANISATIONS

## World Obesity

**Address:**

World Obesity Federation,
Charles Darwin 2,
107 Gray's Inn Road, London,
WC1 X8TZ

**Contact:**

Natasha Joyner
enquiries@worldobesity.org

World Obesity Federation represents professional members of the scientific, medical and research communities from over 50 regional and national obesity associations. Through our membership we create a global community of organisations dedicated to solving the problems of obesity.

Our mission is to lead and drive global efforts to reduce, prevent and treat obesity. We collate, conduct and disseminate world-leading research into obesity, its impact, causes, treatment and prevention. We influence policy of academics, government and business at global, regional and national levels. We bring rigour, consistency and credibility to the field through educational programmes, practical training, publications, conferences and accreditation.

World Obesity offers an internationally recognised online obesity education programme for health professionals, providing evidence-based content developed by leading obesity experts.

www.worldobesity.org

## WCRF International

**Address:**

World Cancer Research Fund International, Second Floor,
22 Bedford Square, London
WC1B 3HH

**Contact:**

international@wcrf.org

World Cancer Research Fund International is the world's leading authority on cancer prevention research related to diet, weight and physical activity. Our vision is to live in a world where no one develops a preventable cancer.

We fund high-quality scientific research into cancer prevention and survivorship and apply it in practical ways to empower people all over the world to take steps to reduce their cancer risk.

We lead and unify a network of cancer charities with a global reach. These cancer charities are based in Europe, the Americas and Asia, giving us a global voice to inform people of cancer prevention. We influence policy at the highest level and are trusted advisers to governments and to other official bodies from around the world.

World Cancer Research Fund International has official relations status with the World Health Organization (WHO).

Visit our Twitter account https://twitter.com/wcrfint and Facebook account https://www.facebook.com/wcrfint to find out more about our work.

# SPONSORS

## American Institute for Cancer Research (AICR)

In 1982, American Institute for Cancer Research (AICR) was founded to advance the simple but then radical idea that cancer could be prevented. AICR has funded over $105 million in research on food, nutrition and physical activity, and the prevention, treatment and survival of cancer. AICR works with its partners in the WCRF network to interpret the results of its research, along with findings from the global scientific community, and craft reliable, evidence-based recommendations for lower cancer risk. For more information on AICR, please visit www.aicr.org.

## World Cancer Research Fund UK (WCRF UK)

For the past 25 years, World Cancer Research Fund UK has been the UK's leading charity dedicated to the prevention of cancer through diet, weight and physical activity. By funding and supporting research, developing policy recommendations and providing health information, we have ensured that people can make informed lifestyle choices to reduce their risk of developing a preventable cancer. As we look forward to our next 25 years, our scientific research ensures that we will continue to have the latest and most authoritative information at our fingertips, all underpinned by independent expert advice.

Our analysis of global research shows that a third of the most common cancers are preventable through a healthy diet, maintaining a healthy weight and regular physical activity.

For more information visit www.wcrf-uk.org
follow us on Twitter at http://twitter.com/wcrf_uk or
visit our Facebook page at http://www.facebook.com/wcrfuk

## Wereld Kanker Onderzoek Fonds (WKOF)

Wereld Kanker Onderzoek Fonds (World Cancer Research Fund Netherlands) has been since 1994 the leading cancer charity in the Netherlands dedicated to cancer prevention through a healthy diet and lifestyle. As part of the global World Cancer Research Fund network we envision a world where no one develops a preventable cancer.

Wereld Kanker Onderzoek Fonds stimulates and funds research into understanding the links between diet, nutrition, physical activity, body composition and cancer. Through our health information programmes we raise awareness for cancer prevention and help people make healthy choices in their diet and lifestyle.

Our driving force: cancer prevention, together we can.

For more information please visit www.wkof.nl

# SCIENTIFIC PROGRAMME

## Thursday 1 September

| | Start Time |
|---|---|
| **Registration** | **07:45** |
| **Welcome, introductions and aims – Chair and WCRF International/ World Obesity Federation** | **09:15** |
| **Session 1. Overview of obesity, physical activity and cancer risk: what do we know and what don't we know?** Chair: Alan Jackson (UK)<br>**Topic 1:** The role of adiposity (including weight change) on cancer risk: epidemiology & molecular mechanisms – **Marc Gunter (France)**<br>**Topic 2:** The role of physical activity on cancer risk: epidemiology & molecular mechanisms – **Michael Leitzmann (Germany)**<br>**Topic 3:** Adiposity (including weight change), physical activity, energy balance and cancer risk: mechanistic evidence from preclinical models – **Stephen Hursting (US)**<br>Facilitated discussion between keynoters and audience. | **09:30** |
| **REFRESHMENTS + Poster session** | **11:30** |
| **Session 2. Setting out methodological issues and novel approaches** Chair: Rudolf Kaaks (Germany)<br>**Topic 1:** Anthropometry: what can we measure and what does it mean? – **Anne McTiernan (US)**<br>**Topic 2:** Novel tools in next-generation epidemiological studies for assessing adiposity and physical activity in cancer research:<br>– Part 1: Imaging approaches – **Jimmy Bell (UK)**<br>– Part 2: Metabolomic biomarker discovery in relation to stratified risk, and personalised medicine – **Marc Gunter (France)**<br>Facilitated discussion between keynoters and audience. | **12:00** |
| **LUNCH + Poster session** | **13:00** |
| **Session 3: Reviewing mechanistic evidence on cancer risk and survival** Chair: Richard Martin (UK )<br>**Topic 1:** Novel method for reviewing mechanistic evidence on diet, nutrition (including body composition) and physical activity and cancer – Sarah Lewis (UK)<br>**Topic 2:** Feasibility study on postmenopausal body fatness and breast cancer<br>– Part 1 – **Eline van Roekel (The Netherlands)**<br>– Part 2 – **Renée Turzanski Fortner (Germany)**<br>Facilitated discussion between keynoters and audience | **14:00** |
| **Session 4: Dedicated session for oral abstract presentations** Chair: Martin Wiseman (UK)<br>**Topic 1:** The effects of caloric restriction on molecular mechanisms related to tumorigenesis in the colon of C57BL/6J mice – **Dieuwertje Kok (The Netherlands)**<br>**Topic 2:** The Novel Adipokine Omentin, Obesity and Colorectal Cancer: New Insights from the EPIC - Potsdam Cohort Study – **Krasimira Aleksandrova (Germany)**<br>**Topic 3:** A study on effect modification by mTOR/PI3K/Akt gene variants of associations between body size, physical activity, early life energy restriction and colorectal cancer risk – **Colinda C. J. M. Simons (The Netherlands)**<br>**Topic 4:** Energy balance-related factors and breast cancer risk in pre- and post-menopausal women – **Doris S. M. Chan (UK)** | **15:00** |
| **REFRESHMENTS + Poster session** | **16:00** |
| **Session 5: How do early life events impact the adiposity/physical activity-cancer relationship?** Co-Chairs: Jennifer Baker (Denmark)<br>**Topic 1:** Early life events and obesity risk: epidemiology – **Marjo-Riitaa Jarvelin (UK)**<br>**Topic 2:** Early life events and cancer risk: epidemiology – **Jennifer Baker (Denmark)**<br>**Topic 3:** The role of height and energy restriction in youth on cancer risk; exploring mechanisms through molecular epidemiology – **Matty Weijenberg (The Netherlands)**<br>Facilitated discussion between keynoters and audience | **16:30** |
| **FINISH** | **17:40** |
| **DRINKS RECEPTION – Sponsored by WKOF** | **18:00** |
| **SPEAKER DINNER – Sponsored by WCRF UK** | **19:00** |

# SCIENTIFIC PROGRAMME

## Friday 2 September

| | Start Time |
|---|---|
| **Registration** | **09:00** |
| **Summary of day 1/ overview of day 2** – Matty Weijenberg (The Netherlands) | **09:20** |
| **Session 6: Obesity, physical activity and cancer survival: what do we know and what don't we know?** Co-Chairs: Wendy Demark-Wahnefried (US)/Matty Weijenberg (The Netherlands)<br>**Topic 1:** Cancer survival: what is the role of body composition pre and post diagnosis? –Ellen Copson (UK)<br>**Topic 2:** Physical exercise interventions in cancer survivors: effects and methodological issues? – Anne May (The Netherlands)<br>**Topic 3:** Impact of weight change on cancer prognosis – Andrew Renehan (UK)<br>**Topic 4:** Weight loss interventions in cancer survivors – Wendy Demark-Wahnefried (US)<br>Facilitated discussion between keynoters and audience | **09:30** |
| **REFRESHMENTS + Poster session** | **11:00** |
| **Session 7: International perspectives on obesity and cancer** Chair: Wendy-Demark Wahnefried (US)<br>**Topic 1:** The impact of obesity on cancer risk in low-middleincome countries – Ellen Kampman (The Netherlands)<br>**Topic 2:** IARC Handbook – Weight management and cancer prevention – Rudolf Kaaks (Germany)<br>Facilitated discussion between keynoters and audience | **11:30** |
| **LUNCH + Poster session** | **12:30** |
| **Session 8: Dedicated session for oral abstract presentations** Chair: Giota Mitrou (UK)<br>**Topic 1:** Body mass index and renal cell cancer: associations with tumour characteristics and overall survival – Alina Vrieling (The Netherlands)<br>**Topic 2:** Lifecourse evolution of body shape and survival after breast cancer in the French EPIC-E3N cohort study – Mathilde His (France<br>**Topic 3:** Serum glucose, triglycerides and cholesterol and prostate cancer survival – Rhonda Arthur (UK)<br>**Topic 4:** Randomised controlled trial of continuous versus intermittent energy restriction during adjuvant chemotherapy (The B-AHEAD2 Trial) – Michelle Harvie (UK) | **13:30** |
| **REFRESHMENTS + Poster session** | **14:30** |
| **Session 9: Policy implications for obesity and physical activity** Co-Chairs: Juan Rivera (Mexico) / João Breda (Denmark)<br>**Topic 1:** Increasing Public Acceptability of Policies tackling Obesity– Theresa Marteau (UK)<br>**Topic 2:** Implementing science into actions for obesity prevention – Juan Rivera (Mexico)<br>**Topic 3:** Facilitating the uptake of policies to promote healthy lifestyles and estimating their impact – Linda Bauld (UK)<br>**Topic 4:** How to balance policies for the prevention of obesity, cancer and other NCDs – Alan Jackson (UK)<br>Roundtable discussion: Chair: João Breda (Denmark), Linda Bauld (UK), Theresa Marteau (UK), Alan Jackson (UK), Martin Wiseman (UK) and Juan Rivera (Mexico) | **15:00** |
| **Session 10: Closing session – Future research directions and concluding remarks** Chair: Marc Gunter (France)<br>**Topic 1:** Cancer and Nutrition NIHR infrastructure collaboration - future research directions – Alan Jackson (UK)<br>**Topic 2:** Conference summary and concluding remarks – Matty Weijenberg (The Netherlands) | **16:15 or 16:35** |
| **FINISH** | **17:05** |

## LEARNING OBJECTIVES

The latest evidence and future research needs will be shared and discussed on topics including:

- The epidemiology and metabolic mechanisms linking obesity, weight change and physical activity to cancer risk and survival.
- Early life events linked to obesity and cancer susceptibility in later life, including discussion on findings on height and cancer risk.
- Issues and new approaches to assess body composition and metabolic markers of cancer risk and progression.
- A novel method for systematically reviewing mechanistic studies, and results from feasibility studies testing this method exploring mechanisms underpinning the links between postmenopausal body fatness and breast cancer.
- Best practice for translating scientific evidence into policy actions for the prevention of obesity as well as cancer and other non-communicable diseases

## SCIENTIFIC COMMITTEE & ABSTRACT REVIEWERS

### Prof. Matty Weijenberg

(Chair), Maastricht University (The Netherlands)

### Dr Marc Gunter

International Agency for Research on Cancer (France)

### Prof. Alan Jackson

University of Southampton (UK)

### Prof. Rudolf Kaaks

German Cancer Research Center (Germany)

### Prof. Jennifer Baker

University of Copenhagen (Denmark)

### Prof. Wendy Demark-Wahnefried,

University of Alabama at Birmingham (US)

### Prof. Juan Rivera

National Institute of Public Health (Mexico)

## SPEAKER & CHAIR BIOGRAPHIES

### Andrew Renehan

Professor Andrew Renehan is professor of cancer studies and surgery at the University of Manchester, and is honorary consultant in Colorectal and Peritoneal Surgical Oncology at the Christie NHS Foundation Trust, Manchester. He is currently the theme research lead for obesity, diabetes and cancer for the Manchester Cancer Research Centre and Farr Institute@HeRC. He is the chair of the international Diabetes and Cancer Research Consortium and the EASD Diabetes and Cancer Study Group. He was one of 21 international scientists in the IARC handbook writing group on Weight control and Cancer, April 2016.

### Anne McTeirnan

Anne McTiernan, MD, PhD is a Full Member at the Fred Hutchinson Cancer Research Center and Research Professor at the University of Washington Schools of Public Health and Medicine in Seattle, Washington, USA.

Her research focuses on diet, obesity, exercise, and risk for cancer development and prognosis. She has published more than 390 scientific manuscripts, and the book, Breast Fitness (St. Martin's Press, 2000). Committee work includes the WCRF/AICR expert panel, the 2008 U.S. Physical Activity Guidelines, IARC, and the American Cancer Society. Dr. McTiernan's forthcoming memoir is Starved: A Nutrition Doctor's Journey from Empty to Full (Central Recovery Press).

### Anne May

Dr. Anne May is working at the Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht in The Netherlands.

She holds a Master's degree in Epidemiology and in Human Movement Sciences (with distinction). During her PhD studies she was involved in a randomized controlled trial on effects of exercise and cognitive behavioral therapy on cancer patients' quality of life. After obtaining her PhD degree in 2008, she continued working in the field of exercise-oncology.

She is currently the principal investigator of several multicenter RCT investigating the effects of exercise in patients with breast, colon and esophageal cancer. She is interested in effects of exercise, in the mediators of the effect and also in methodological aspects related to exercise-oncology research. For the latter she received a personal VENI grant for talented and creative researchers to study a novel research design and methodology for exercise-oncology RCTs ((The Netherlands Organisation for Health Research (ZonMw)).

### Eline van Roekel

Dr. van Roekel is a postdoctoral researcher within cancer and molecular epidemiology at the Department of Epidemiology at Maastricht University, the Netherlands.

During 2011-2015, she conducted her PhD research on associations of physical activity and sedentary behaviour with quality of life in colorectal cancer survivors. For her PhD thesis, she used data from a new observational study in colorectal cancer survivors that she initiated together with her supervisors at Maastricht University: the Energy for life after ColoRectal cancer (EnCoRe) study. During her PhD, she obtained a WCRF fellowship to attend the International Course in Nutritional Epidemiology at Imperial College London, and a travel grant from the Dutch Cancer Society to conduct a 2-month work visit to the University of Queensland in Australia.

Since obtaining her PhD degree in December 2015, dr. van Roekel has continued to work on studying associations of lifestyle factors with quality of life of colorectal cancer survivors within the EnCoRe study. In addition, she aims to develop herself as a molecular epidemiologist by studying biological mechanisms linking associations of lifestyle with cancer etiology and quality of life outcomes in cancer survivors. For this purpose, she performed a work visit to the International Agency for Research on Cancer in Lyon in September 2015 to learn about metabolomics and the application in epidemiological research. In November 2015, she started working on a WCRF-funded project aiming to validate a systematic review framework for integrating evidence from human, animal, and other mechanistic studies on biological mechanisms linking lifestyle with cancer.

# SPEAKER & CHAIR BIOGRAPHIES

## Ellen Copson

Dr Copson is Associate Professor and honorary consultant in Medical Oncology at the University of Southampton, where she specialises in treating breast cancer.

Dr Copson is particularly interested in genomic and modifiable host factors that influence the outcome of early breast cancer. She is a lead researcher on the POSH study, a large national cohort study of young breast cancer patients and principal investigator of several cohort studies exploring body composition in breast cancer. She is principal investigator for many clinical trials in early and advanced breast cancer.

Dr Copson is a member of the NCRI Breast Clinical Studies Group and is Cancer lead of the Wessex Genomic Medical Centre.

## Ellen Kampman

Ellen Kampman is a nutritional epidemiologist and Chair in Nutrition and Disease at Wageningen University, the Netherlands.

Her research focuses on the role of lifestyle in cancer prevention and prognosis. Her group conducts observational and intervention studies in high and low/medium income countries. She has published more than 150 papers, is a member of (inter)national advisory and scientific committees, and is senior editor of the AACR journal Cancer Epidemiology Biomarkers and Prevention.

Prof. Kampman studied Nutrition and Health at Wageningen University, was a visiting fellow at the Boston Harvard School of Public Health and received postdoctoral training at the Fred Hutchinson Cancer Research Centre in Seattle.

## Giota Mitrou

Dr Panagiota Mitrou has an MSc in Genetic Manipulation & Molecular Biology from the University of Sussex and a PhD in Genetic Epidemiology from Cambridge University. She was a visiting postdoctoral fellow at the Division of Cancer Epidemiology and Genetics at the National Cancer Institute, USA and a Research Associate at the MRC Centre in Nutritional Epidemiology for Cancer Prevention and Survival (CNC), Department of Public Health and Primary Care, Cambridge University, UK.

Dr Mitrou is currently the Director of Research Funding and Science External Relations at WCRF International with main responsibilities to provide strategic direction for the science activities of the WCRF network (UK, HK, NL) and expand WCRF International's global positioning and influence through strategic partnerships at national and international level.

She teaches on the Nutritional Epidemiology Course at Imperial College London and is a Visiting Lecturer for the MSc course in Nutrition at University College London and the University of Reading.

## Jennifer Baker

Dr. Jennifer L. Baker is an Associate Professor at the University of Copenhagen and is affiliated with the Institute of Preventive Medicine in Denmark. Jennifer is internationally recognized for her work on the short- and long-term consequences of childhood body size and growth.

Jennifer's group has established that childhood body size and growth are differentially associated with adult diseases, including several forms of cancer, cardiovascular disease and type 2 diabetes. Jennifer serves on many scientific committees for Danish and European projects and is the co-chair of the Childhood Obesity Task Force for the European Association for the Study of Obesity.

## Jimmy Bell

After completely his PhD Professor Jimmy D Bell joined the MRC (Imperial College London). As a Group Head he worked extensively on the application of in vivo MR methodologies for the study of disease development, demonstrating for the first time the importance of gene-environment interaction in obesity. Moved to the University of Westminster establishing the Research Centre for Optimal Health. He has published over 200 peer-reviewed papers and book chapters. His research program aims to define the influence of candidate genes and environmental factors on optimal health and chronic diseases, particularly those associated with obesity and accelerated ageing.

## João Breda

João Breda has a PhD in Nutritional Sciences from Porto University. He also graduated in Nutritional Sciences at Porto University. He has a Master's Degree in Public Health from the Medical Sciences Faculty of the University Nova de Lisboa and an MBA from the European University in Barcelona.

Dr Breda is the Programme Manager: Nutrition, Physical Activity and Obesity at WHO Regional Office for Europe and responsible for providing support to the 53 Member States of the WHO European Region on the implementation of the European Charter on Counteracting Obesity and the Vienna Declaration on Nutrition and Noncommunicable Diseases as well as evaluating their progress implementation. His team is leading for the largest and most comprehensive childhood obesity surveillance mechanisms globally and developed the new European Food and Nutrition Action Plan 2015-2020 and the first European Physical Activity for Health Strategy.

In Portugal, João Breda worked as a Public Health Nutritionist at the General Health Directorate and ARS Centro having launched and led for several years the National Platform Against Obesity. Published in scientific journals and presented in national and international congresses, several dozens of papers and also published several original books. He was Researcher and Professor of Nutrition at Universidade Atlântica and Head of Department of the Nutritional Sciences where he developed and implemented the first Nutritional Sciences Bachelor. He also had academic functions at Algarve University, Higher School of Agriculture in Coimbra and the Tourism and Hospitality School of Coimbra.

## Juan Rivera

Dr. Juan A. Rivera is Founding Director of the Center for Research in Nutrition and Health at the National Institute of Public Health and Professor of Nutrition at the School of Public Health in Mexico. He is member of the National Academy of Medicine, the Latin American Society of Nutrition (SLAN) and the American Society of Nutrition, the WCRF International Policy Advisory Group, the World Obesity/ Public Prevention Steering Committee, the HLPE on Food Security and Nutrition and is President of SLAN.

Dr. Rivera earned both his master's and doctorate degrees in International Nutrition from Cornell University. His research interests include the epidemiology of malnutrition in all its forms, the study of risk factors of malnutrition (infant feeding practices and diet); the generation of evidence to guide the design of policy and programs for the prevention of undernutrition, obesity and NCCDs; and the evaluation of those policies.

## Linda Bauld

Linda Bauld holds the Cancer Research/ BUPA Chair in Behavioural Research for Cancer Prevention. This role involves providing leadership for CRUK's cancer prevention initiative and is combined with her position as Professor of Health Policy and Dean of Research at the University of Stirling. She is also Deputy Director of the UK Centre for Tobacco and Alcohol Studies, a UKCRC Centre for Public Health Excellence that covers 13 Universities.

Linda has a background in applied policy research and for the past 17 years her research interests have centred on the evaluation of public health interventions. She has conducted studies on drug and alcohol use, inequalities in health and, most notably, on tobacco control and smoking cessation. She is a former scientific adviser on tobacco control to the UK government and recently led the development of an independent alcohol strategy for the UK, 'Health First'. Her CRUK role involves working across health behaviours to build capacity in cancer prevention research in the UK and beyond.

# SPEAKER & CHAIR BIOGRAPHIES

## Marc Gunter

Marc Gunter is Head of the Section of Nutrition and Metabolism at the International Agency for Research on Cancer (IARC), the specialized cancer research agency of the World Health Organization.

Dr Gunter holds a PhD in molecular epidemiology from the University of Cambridge and a degree in biochemistry from the University of Oxford. He completed his postdoctoral training at the U.S National Cancer Institute and has held faculty positions at the Albert Einstein College of Medicine in New York and Imperial College London. His research focuses on the role of nutrition and obesity in the natural history of cancer with an emphasis on metabolic dysfunction and in particular the insulin/IGF/mTOR pathway.

Dr Gunter is principal investigator of a number of studies applying high dimensional metabolic profiling within the framework of large prospective and clinical cohorts to identify novel biochemical pathways involved in cancer development and prognosis. Recent publications include investigations of obesity subtypes defined by metabolic measurements in relation to breast and colorectal cancer risk, adipose tissue-derived factors and breast cancer and the role of endogenous oestrogens in colorectal cancer development.

## Marjo-Riitaa Jarvelin

Marjo-Riitta Järvelin is Professor and Chair in Lifecourse Epidemiology at Imperial College London, UK (since 2002), also holding a visiting professorship at Brunel University London, UK and a part-time professorship at the University of Oulu, Finland. She is honorary consultant for Imperial College Healthcare NHS Trust, UK. She has been running large-scale population based studies for over 25 years, working on the genetic and early life environmental origins of multi-factorial diseases and disorders, in close collaboration with many international institutions, groups and networks. She is a Scientific Director of the Northern Finland Birth Cohort (NFBC) research programme (about 20 000 subjects, born in 1966 and 1985-86 and their 35,000 parents), and have an active role in research training as Director of Postgraduate Studies at School of Public Health, Imperial College London. Professor Jarvelin has published over 600 original papers and supervised 29 PhD students until completion and many other postgraduate theses. She has received funding from MRC UK, Welcome Trust UK, ESRC UK, the EU (FP5, FP7 and Horizon 2020), NIH USA and Academy of Finland among others. She has been nominated on several prestigious visiting and collaboration awards for e.g. China, Russia, Korea, USA, UK and New Zealand. In 2007-8, she received an award of Excellence in Genetic Epidemiology at Imperial College London. In 2012, I was honoured by the title, Epidemiologist of the Year in Finland and in 2013 was invited to join, as a member, the Finnish Academy of Sciences.

## Martin Wiseman

Professor Martin Wiseman is currently an independent nutrition consultant, and Medical and Scientific Adviser at the World Cancer Research Fund International. In addition, he is a visiting professor in human nutrition at Southampton University. He was project director for the 2007 WCRF/AICR expert report Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective, and its 2009 companion Policy and Action for Cancer Prevention.

Until 1999 he was head of the Nutrition Unit at the Department of Health, where he had responsibility for nutrition science, including the work of COMA, the Committee on Medical Aspects of Food and Nutrition Policy; for nutrition surveys; and for advising on and implementing nutrition policy.

He qualified from Guy's Hospital in London in 1975. He became a member of the Royal College of Physicians in 1977 and followed a traditional career path as a general physician until 1981 when he developed an interest in clinical research. He has published papers on diabetes and kidney function and the effects of nutrition on them. He moved to the Department of Health in 1986 but still retains an appointment within the NHS, where he continues with clinical activities in a diabetes clinic.

He was Honorary External Relations Officer of the Nutrition Society from 2001 to 2006, and was Honorary Treasurer of the Association for Nutrition until 2014. He is Chair of the Management Team of the Intercollegiate Group on Nutrition of the Academy of Medical Royal Colleges, and is a Fellow of the Royal College of Physicians, of the Royal College of Pathologists, and of the Association for Nutrition.

## Matty Weijenberg

Matty Weijenberg is a professor of Molecular Epidemiology of Cancer at the department of Epidemiology and the GROW-School for Oncology and Developmental Biology at Maastricht. Her field of research evolves around the molecular epidemiology of colorectal cancer, specifically the role of nutrition, physical activity, body composition, early life exposures, gene-environment interaction, (epi)genetics, in the aetiology of colorectal cancer; and more recently, the quality of life and prognosis of colorectal cancer survivors.

Over the past 20 years she has developed a research line on the molecular epidemiology of colorectal cancer which is embedded within a large prospective cohort study, The Netherlands Cohort Study on diet and cancer, and has resulted in a comprehensive molecular databases of colorectal cancer patients from a prospective study. This enables the study of 1) the aetiology of colorectal cancer according to (epi)genetic characteristics of tumors, 2) gene-environment interactions and risk of colorectal cancer, 3) (epi)genetic characteristics in a large unselected sample of colorectal cancer tumors, 4) (epi)genetic markers of tumors and (long-term) prognosis of colorectal cancer cases.

In 2012, she set up a cohort of colorectal cancer survivors in the Southern part of the Netherlands, the ongoing Energy for life after ColoRectal cancer (EnCoRe) study, to investigate the role of lifestyle factors for the quality of life, other patient reported outcomes, and prognosis of colorectal cancer survivors.

## Michael Leitzmann

Michael Leitzmann's main research interests involve the relations of diet, body size, and physical activity to the development of chronic diseases.

He holds an MD from the University of Berlin and an MPH and a DrPH from the Harvard School of Public Health. He currently serves as chair of the Department of Epidemiology and Preventive Medicine at the University of Regensburg, Germany. He was previously appointed as investigator at the U.S. National Cancer Institute. He serves as a member of several journal editorial boards and as an expert reviewer for numerous international research organisation.

## Renee Turzanski Fortner

Renée Turzanski Fortner (Ph.D.) is a scientist at the German Cancer Research Center (DKFZ) in Heidelberg, Germany.

Dr. Fortner's primary research focus is on risk factors for breast, ovarian, and endometrial cancers and integrating novel biomarkers into epidemiologic research. She completed a postdoctoral fellowship at Harvard University with the Nurses' Health Study (NHS) and NHSII, and has extended that experience to investigations in the European Investigation into Cancer and Nutrition (EPIC) cohort and the Finnish and Northern Sweden Maternity Cohorts in her current position at the DKFZ.

## Richard Martin

Richard Martin is currently Professor of Clinical Epidemiology in the School of Social and Community Medicine, University of Bristol. He qualified in Medicine from the University of Nottingham, trained and worked as a GP, and then built on an interest in epidemiology (that was first sparked during his intercalated BMedSci at Nottingham) by doing the MSc in Epidemiology at the London School of Hygiene and Tropical Medicine. He subsequently moved to Bristol to take up a Lecturer post and then a Wellcome Trust Research Training Fellowship in Clinical Epidemiology, and have worked at the School of Social and Community Medicine ever since.

## Rudolf Kaaks

Rudolf Kaaks received his Master of Science in Human Nutrition & Epidemiology at the University of Wageningen in 1987 and his PhD in Nutritional Epidemiology in 1994. Within his scientific career he worked as epidemiologist at the International Agency for Research on Cancer(IARC), Lyon (1988-2001) where he contributed to the development of the European EPIC project. In 2001 he became head of the Hormones and Cancer Group at IARC. In 2006 Rudolf Kaaks was appointed Professor (Chair, Cancer Epidemiology) at the University of Heidelberg and head of the Division of Cancer Epidemiology at the German Cancer Research Center (DKFZ), Heidelberg, Germany.

From 2009 to 2015 he was member of the Board of Scientific Directors of the German National Cohort (NaKo). In September 2015 he became speaker of Research Program C Cancer Risk Factors and Prevention"

# SPEAKER & CHAIR BIOGRAPHIES

## Sarah Lewis

I obtained a BSc in Genetics at the University of Sheffield in 1995 and then went on to complete a PhD in Genetic Epidemiology at the University of Manchester in 1999. I then had a series of short postdoctoral positions including a post at the International Agency for Research on Cancer. I joined the School of Social and Community Medicine in January 2004 as a lecturer in Genetic Epidemiology and was promoted to Senior Lecturer in 2009.

My research interests are in using Mendelian Randomization to understand risk factors for cancer and also to identify key nutrients required for in utero development. I am involved in a large UK wide cohort study of cleft lip and palate, and a large birth cohort in which I am looking at the role of nutrition during pregnancy on childhood IQ and behaviour. I co-lead a work package on Mendelian Randomisation for the Integrative Cancer Epidemiology Programme, which is funded by Cancer Research UK. I am a principal investigator on a project to develop a framework for systematic reviews of mechanistic studies of nutrition and cancer in collaboration with the World Cancer Research Fund. I also hold a grant from the WCRF to apply the above framework and Mendelian randomization to understanding the role of diet in prostate cancer.

## Stephen Hursting

Dr. Stephen Hursting is Professor and Director of the Division of Nutritional Biochemistry in the Department of Nutrition at the University of North Carolina (UNC) at Chapel Hill. He is also Professor at the UNC Nutrition Research Institute and a member of the UNC Lineberger Comprehensive Cancer Center. He earned his PhD in nutritional biochemistry and MPH in nutritional epidemiology from UNC-Chapel Hill, and he completed postdoctoral training in molecular carcinogenesis and cancer prevention at the National Cancer Institute (NCI).

Prior to joining the UNC faculty in 2014, Dr. Hursting was Professor and Chair of the Department of Nutritional Sciences at the University of Texas (UT) at Austin, the McKean-Love Endowed Chair of Nutritional, Molecular and Cellular Sciences in the UT College of Natural Sciences, and Professor of Molecular Carcinogenesis at the UT-MD Anderson Cancer Center (2005-14). He also previously served as Chief of the NCI's Nutrition and Molecular Carcinogenesis Laboratory Section (1999-2005). His research interests center on diet-gene interactions relevant to cancer prevention, particularly the molecular and metabolic mechanisms underlying obesity- cancer associations, and the interplay between obesity, metabolism and cancer.

Primarily using preclinical models (including human and mouse cell lines and genetically engineered mouse models of cancer) in parallel with human studies, he is currently focusing on the molecular and metabolic changes occurring in response to lifestyle-based (dietary and physical activity), or pharmacologic manipulation of energy metabolism and cell signaling pathways, with emphasis on the insulin/IGF-1 signaling pathways as well as inflammation.

## Theresa Marteau

Professor Theresa Marteau is Director of the Behaviour and Health Research Unit in the Clinical School at the University of Cambridge, and Director of Studies in Psychological and Behavioural Sciences at Christ's College, Cambridge. She studied psychology at the LSE and the University of Oxford.

Her research interests include:

- development and evaluation of interventions to change behaviour (principally diet, physical activity, tobacco and alcohol consumption) to improve population health and reduce health inequalities, with a particular focus on targeting non conscious processes
- risk perception and communication particular of biomarker-derived risks, and their weak links with behaviour change
- acceptability to public and policy makers of government intervention to change behavior.

She is a Fellow of the Academy of Medical Sciences and the Academy of Social Sciences.

## Wendy Demark Wahnefried

Wendy Demark-Wahnefried, PhD, RD is Professor and Webb Endowed Chair of Nutrition Sciences at the University of Alabama at Birmingham (UAB).

Her career in cancer research began at Duke University where she was on faculty for 17 years, then was recruited to MD Anderson, and then to the UAB Comprehensive Cancer Center in 2010 as Associate Director for Cancer Prevention and Control. Her research in nutrition and cancer control has produced >200 scientific publications, and recognition as a Komen Professor of Survivorship and an American Cancer Society (ACS) Clinical Research Professor. Dr. Demark-Wahnefried serves on the ACS Guidelines Panel for Nutrition and Physical Activity, American Society of Clinical Oncology Committees on Cancer Survivorship and Energy Balance, Institute of Medicine's National Cancer Policy Forum, and others. She has led several diet and exercise intervention trials in cancer survivors including FRESH START and Reach-out to EnhancE Wellness (RENEW) in Older Survivors.



# SPEAKER ABSTRACTS

## The role of adiposity (including weight change) on cancer risk: epidemiology & molecular mechanisms – Marc Gunter (France)

Adiposity, assessed either by body mass index (BMI) or waist circumference, is now an established positive risk factor for cancers of the colon and rectum, gastric cardia, liver (hepatocellular carcinoma), gallbladder, pancreas, kidney (renal cell carcinoma), endometrium, postmenopausal breast, ovary, thyroid, meningioma, multiple myeloma and adenocarcinoma of the oesophagus. Obesity is associated with significant metabolic and endocrine abnormalities including alterations in sex hormone metabolism, insulin signalling, and adipokines/inflammatory pathways. All three mechanisms influence the balance between cell proliferation and apoptosis and have been linked to cancer development in both experimental and observational studies. There is generally convincing evidence that intentional body-weight loss positively affects these key mechanisms; however, it is likely that other, hitherto unrecognised molecular pathways mediate the adiposity-cancer association. In this presentation I will summarize the existing epidemiologic literature on adiposity and cancer development as well as the underlying molecular mechanisms, highlighting areas of uncertainty that require further investigation.

## The role of physical activity on cancer risk: epidemiology & molecular mechanisms – Michael Leitzmann (Germany)

There is strong evidence that physical activity is related to decreased risks of colon, breast, and endometrial cancers, whereas the evidence for a protective effect of physical activity on other cancer sites is limited. There are only sparse data regarding the proportion of cancer occurrences that can be attributed to lack of physical activity, but insufficient physical activity levels have been estimated to cause 9% of breast cancer cases and 10% of colon cancer cases in Europe. Distinguishing the preventability estimates of physical activity from those related to weight control is challenging because body mass is related to both physical activity and to cancer. Physical activity may influence cancer risk through beneficial effects on insulin resistance, sex hormone metabolism, inflammatory cytokines, immune function, prevention of oxidative damage, and upregulation of DNA repair mechanisms. By comparison, effects of physical activity on growth factor concentrations and their binding proteins are less clear. The primary challenges in deriving recommendations for physical activity lie in our lack of knowledge regarding which specific type, intensity, frequency, and duration of physical activity is necessary to reduce cancer risk. Future research should be directed at clarifying the etiologic pathways underlying the relation of physical activity to carcinogenesis; gaining a better understanding of the etiologically relevant time period of exposure to physical activity during life that potentially counteracts cancer risk; improving methods for assessing physical activity in large-scale population studies; and increasing our knowledge concerning a possible link between physical activity and improved cancer survival.

## Energy Balance, Adiposity and Cancer: Mechanistic Evidence from Preclinical Models – Stephen D. Hursting, PhD, MPH (US)

The prevalence of obesity, an established risk factor for many cancers, has increased dramatically over the past 40 years in the US and many other countries. Relative to normoweight cancer patients, obese cancer patients often have poorer prognoses, resistance to chemotherapies and are more likely to develop distant metastases. Recent progress on elucidating the mechanisms underlying the obesity- cancer connection suggests that obesity exerts pleomorphic effects on pathways related to tumor development and progression, and thus there are multiple opportunities for primary to tertiary prevention of obesity-related cancers. We know from preclinical studies that obesity can impact each of the well-established hallmarks of cancer, and obesity-associated perturbations in systemic metabolism and inflammation, and the interactions of these perturbations with cancer cell energetics, are emerging as the primary drivers of obesity-associated cancer development and progression. Several obesity-related host factors, including components of the secretome and structural components of the tumor microenvironment, are extrinsic to, and interact with, the intrinsic molecular characteristics of cancer cells (including cancer stem cells), and each will be considered in the context of potential preventive and therapeutic strategies to reduce the burden of obesity-related cancers. Moreover, the impact and underlying mechanisms of obesity reversal via calorie restricted diets, physical activity or surgical interventions in a preclinical breast cancer model will be discussed.

## Anthropometry: what can we measure and what does it mean? – Anne McTiernan (US)

Increased body size and adiposity are associated with increased risk for several cancers, and for reduced survival in those diagnosed with cancer. While body size in adults has been operationally defined by the World Health Organization by level of body mass index (BMI, kg/m$^2$), the underlying issue for

carcinogenesis and prognosis is likely the biological effects of excessive stores of adipose tissue. Relatedly, muscle and bone mass may also affect risk for cancer development and prognosis. Several methods of measuring adiposity and body composition in humans have been used in clinical trials and observational studies related to cancer etiology, prevention, and survivorship.

This talk will review several measures of overall body composition and specific depots of adipose tissue including: weight, height, BMI, body circumferences, dual-energy X-ray absorptiometry (DXA), computed tomography (CT), and magnetic resonance imaging (MRI). Measurement properties will be discussed, as well as systematic error from self-reported measures. The utility of standard cut-points for measures vs. study-specific categorizations will be presented. Examples from observational studies and clinical trials will be provided.

Adipose tissue can be sampled in humans to examine histology, and to measure cancer-related biomarkers such as adipokines and gene expression. Subcutaneous adipose tissue can be sampled from most areas of the body, while visceral fat has been obtained in conjunction with surgical procedures, and fat within and around muscle and organs is less accessible. Examples from our studies of weight loss effects on subcutaneous abdominal and breast adipose tissue biology will be given.

## Novel tools in next-generation epidemiological studies for assessing adiposity and physical activity in cancer research: Imaging approaches – Jimmy Bell (UK)

As rates of obesity and associated disease escalate globally, the role of body adiposity is eliciting growing interest. For example, it has been known for some time that coronary heart disease (CHD), type II diabetes and some forms of cancer are linked to total adiposity. However, traditional methods to assess adiposity do not account for all people who develop these diseases. Indeed, recent studies have showed that the mortality in individuals with a BMI <25 was comparable to those with a BMI > 25. Furthermore, a number of epidemiological and interventional studies have also shown that significant improvements in metabolic profile can be obtained in the absence of changes in BMI or anthropometric measures. These improvements appear to be related to changes within specific fat-depots, in particular abdominal and ectopic fat. It is clear that more robust and reproducible method are needed. In this presentation we will explore the value of more direct imaging techniques, including the current "gold-standard" MRI, for obtaining accurate and reproducible measurements of body fat content and distribution. We will discuss how for example the widely reported correlation between BMI and total body fat content masks significant variations in the relationship between BMI and body fat content/distribution. Similarly, waist circumference (WC) and WHR, commonly used to complement BMI, have also been shown to have considerable inter-individual variation in their estimation of fat distribution. Thus, regardless of the accumulating evidence these techniques continue in many cases to be the methods of choice. This appears to be driven mainly by convenience rather than relevance.

## Novel tools in next-generation epidemiological studies for assessing adiposity and physical activity in cancer research: Metabolomic biomarker discovery in relation to stratified risk, and personalised medicine – Marc Gunter (France)

Metabolomics is the measurement of small metabolites in biological samples that represent end products of a variety of metabolic and cellular pathways. It is a powerful new approach to capture biomarker information on a range of disease processes as well as host responses to exogenous and endogenous exposures. As an emerging approach used in epidemiologic and clinical studies, metabolomics has the potential to improve cancer risk assessment, screening, diagnosis, prognosis and predictive response to therapy, as well as to provide mechanistic insights. In this presentation I will outline the major concepts underlying the application of metabolomics to population-based study designs with specific reference to risk stratification and personalized interventions and will provide examples from recent and ongoing studies from our group.

## Novel method for reviewing mechanistic evidence on diet, nutrition (including body composition) and physical activity and cancer – Sarah Lewis (UK)

**Background:** Many laboratory experiments are performed to identify causal pathways and in doing so inform human health. These mechanistic studies complement epidemiological findings and can offer insights into biological plausibility and pathways between exposure and disease. Systematic reviews are the most robust way to synthesise data which have addressed a common question. However, such methods are lacking for mechanistic studies.

**Methods**: A multidisciplinary team with expertise in informatics, statistics, epidemiology, systematic reviews, cancer biology and nutrition was assembled. A series of 5 one-day workshops took place involving presentations, group work and discussions, along with smaller meetings and research being carried out in the intervening periods.

**Results:** We have developed a two stage framework, the first stage of which is a mechanisms discovery stage, followed by a targeted systematic review of studies on a specific mechanism. In doing this we overcame many challenges including: developing an automation tool to deal with the vast amount of data generated in the first stage, developing strategies for assessing the quality, relevance and likelihood of publication bias among animal and cell studies, displaying disparate data and integrating data from a variety of study types.

**Conclusion:** The above template will be available to researchers in the future who wish to conduct robust systematic reviews of the mechanisms which underpin associations between exposures and cancer.

**Funding:** World Cancer Research Fund (WCRF)

## Applying and evaluating a novel systematic review framework to integrate mechanistic studies linking body fatness with (postmenopausal) breast cancer: Results from the Maastricht Team – Eline van Roekel (The Netherlands)

Although several mechanisms have been proposed to underpin the body fatness-postmenopausal breast cancer association, no systematic review of mechanistic studies has been performed to date. In this study, we have used the systematic review framework that was developed by WCRF International/University of Bristol to summarize the literature on potential mechanisms linking body fatness to breast cancer (**stage 1**), and conduct a systematic review of existing mechanistic evidence on the role of the insulin-like growth factor 1 receptor (IGF1R) in linking body fatness to (postmenopausal) breast cancer (**stage 2**). For stage 1, we have performed an extensive literature search to identify studies linking body fatness and/or breast cancer to (breast) cancer-mechanisms. The Text Mining for Mechanism Prioritization (TeMMPo) tool was used to generate a comprehensive overview of potential mechanisms and scores were calculated for the amount of evidence for specific mechanisms. For stage 2, we searched the literature for mechanistic studies linking body fatness to IGF1R, and IGF1R to breast cancer. Two independent reviewers selected articles based on predefined in- and exclusion criteria. The quality of the included studies (n=35) was assessed by study type-specific risk-of-bias tools and data from different types of studies were synthesized and integrated. Results showed that the current evidence on IGF1R as a potential mechanism linking body fatness to breast cancer is weak and that more mechanistic studies are necessary. We think the framework is the start of a discussion on how to integrate evidence from different research streams and can provide guidance on this process.

## Feasibility study on postmenopausal body fatness and breast cancer: Testing a Novel Framework for Identification and Evaluation of Biologic Mechanisms in Chronic Disease: Body fatness and breast cancer – Renée Turzanski Fortner (Germany)

We tested the feasibility of the World Cancer Research Fund (WCRF) International/University of Bristol's two-stage framework: "Linking diet, nutrition and physical activity to cancer: a systematic review framework for integrating evidence from human, animal, and other mechanistic studies" to (1) identify biological mechanisms underpinning the link between body fatness and postmenopausal breast cancer, and (2) systematically review and assess the strength of the evidence for an association between the insulin-like growth factor 1 receptor (IGF1R) and breast cancer. In Stage 1, we employed the "Text Mining for Mechanism Prioritisation" (TeMMPo) tool to identify intermediate mechanisms linking body fatness to postmenopausal breast cancer; pathways identified included sex steroids, insulin signalling, and lipids. The Stage 2 systematic review of IGF1R expression/signalling as an intermediate mechanism was based on 693 unique references identified in PubMed: 262 including the search terms for body fatness and IGF1R (i.e., exposure (E) to intermediate phenotype (IP)) and 431 including the search terms for IGF1R and breast cancer (i.e., IP to outcome (O)). Of the identified reports, 26 E to IP (10%) and 123 IP to O (9.3%) articles were selected for full-text data extraction and assessment. Based on the GRADE assessment and our appraisal of the literature, we found inconclusive evidence for an association between body fatness and IGF1R expression/signalling and modest evidence linking IGF1R expression/signalling to breast cancer. Considering the overall body of evidence, we conclude that there is weak evidence for signalling via the IGF1R as a pathway linking body fatness to breast cancer.

# SPEAKER ABSTRACTS

## Early life events and obesity risk: epidemiology – Marjo-Riitaa Jarvelin (UK)

Childhood and adolescent overweight and obesity, which are leading causes of early type 2 diabetes and cardiovascular disease, have become major public health concerns both in westernized and, more recently, in developing countries. Traditional approaches for the management of overweight and obesity have had poor long-term efficacy. Therefore prevention is currently the most promising strategy for controlling the obesity epidemic. However, much research is needed in order to understand better the critical life-course "windows" for effective prevention. Several socio-demographic and anthropometric predictors, as well as several common genetic variants, have been associated with obesity development. Some longitudinal studies have shown a strong association between early infancy weight gain rate or adiposity and childhood as well as adult body weight, fat mass and body mass index (BMI). In Northern Finland Birth Cohort studies we have aimed to build algorithms for the early identification of clinical, socio-demographic and genetic risk factors that predict obesity development. Our extensive studies on childhood overweight/obesity show for the first time that a set of readily available risk factors relating to maternity/child welfare care at birth- parental BMI, birthweight, gestational weight gain, health behaviour and social indicators – are good predictors of child and adolescent overweight/obesity, while currently known genetic variants make a smaller contribution. Results of this research and the related online obesity calculator could easily be implemented after further testing into clinical practice (http://files-good.ibl.fr/childhood-obesity/). Our striking observation was that 20% of the cohort predicted to have the highest risk at birth make up to 80% of all those obese at age 16y. We have also confirmed the promising usefulness of the identified socio-demographic and anthropometric factors in other independent cohorts from the USA and Italy. Furthermore, to better understand the interplay of potential risk and protective factors, we have used longitudinal data modeling, which takes into account the temporal relationships of and the interactions with environmental variables. We were able to show that multiple prenatal, birth, adolescent and adult factors predicted BMI level independently of each other at various stages in life course. Studies also show that early life stress may modify the association between genetic variants and fetal growth, and that both may have impact on metabolic health later in life. Recent research suggests that assessment of the risk for future overweight or obesity in very early life may be a basis for focused preventive interventions for at-risk individuals. Huge advances in genetic, epigenetic and analytical technologies will make it possible to use increasingly multifaceted life-course data to better understand the mechanisms and roles of genes and the environment in disease development from early stage of life.

## Early life events and cancer risk: epidemiology – Jennifer Baker (Denmark)

A large and growing body of epidemiological literature links early life events to cancer risk later in life. A brief overview of early life risk factors for adult cancer, spanning from the prenatal period through early adulthood will be presented. A review of the evidence linking childhood body size and growth, as an indicator of the later risk of cancer, will be provided. A focus will be placed on evidence from the Copenhagen School Health Records Register, which is a unique electronic resource of 372.636 children with measured heights and weights who are followed-up for outcomes such as cancer through national health registers. Results from ongoing studies will be presented as an illustration of how childhood body size is emerging as a strong indicator of risk for adult cancer. And finally, a discussion of emerging areas such as gene-environment interactions and the intergenerational transmission of cancer risk in the context of early life factors, among other future research directions, gaps and priorities will be discussed.

## The role of height and energy restriction in youth on cancer risk; exploring mechanisms through molecular epidemiology – Matty Weijenberg (The Netherlands)

Adult attained height is an established risk factor for cancer risk at several sites. The most convincing evidence has been reported for postmenopausal breast cancer and colorectal cancer risk. For every 5 cm increase in height, postmenopausal breast cancer risk is reported to be increased by 7 to 11% and colorectal cancer risk is increased by 6 to 11% in women and 4 to 9% in men. Height in itself is probably not causally related to cancer, but rather a consistent marker for one or more factors and/or mechanisms that influence growth in relation to both height and cancer risk. Height is determined in the first 20 years of life by aggregated genetic and environmental components, which determine growth in childhood and adolescence but may also spur neoplastic growth later in life. Although adult attained height is not a likely target for intervention to reduce cancer risk, understanding how height is associated to cancer is essential to expand our knowledge concerning the pathways that lead to cancer development later in life. The similarity of the height-associated risks for different cancer sites in different populations suggests that common mechanisms are at play, in part environmental mechanisms involved in early life and in part genetically determined mechanisms. Both mechanisms will be discussed in more detail, specifically (severe) energy restriction in early life and the role of genetic variants in further unravelling the underlying mechanisms linking height to cancer risk.



## Cancer survival: what is the role of body composition pre and post diagnosis? – Ellen Copson (UK)

High body mass index (BMI) is associated with an increased risk of breast cancer in post-menopausal women but poorer outcomes in all age groups. The underlying mechanism is likely to be multi-factorial. Patients with a high BMI tend to present later due to their body habitus. Some studies have also indicated an increased incidence of biologically adverse features, including ER negative tumours, in obese patients. Surgical complications occur with a higher incidence in obese patients, potentially delaying systemic therapies, and reports suggest that both chemotherapy and endocrine therapy are less effective in patients with BMIs of 30 kg/m$^2$ or greater. High BMI is generally interpreted as excess adiposity and a World Cancer Research Fund report judged that the associations between BMI and incidence of breast cancer were due to body fatness. However, BMI cannot distinguish lean mass from fat mass, or characterise body fat distribution, and so individuals with the same BMI can have different body composition. Most chemotherapy drugs are dosed according to calculated body surface area (BSA). Patients with a similar BSA or BMI may have wide variations in their distribution of adipose tissue and skeletal muscle (body composition); however few studies have looked at the effect of this on chemotherapy tolerance. Finally, adjuvant treatments for breast cancer can themselves result in body composition changes.

In this presentation I will discuss data from the Southampton based POSH and CANDO-2 studies to illustrate the complex effects of body composition on the presentation, treatment and outcome of early breast cancer.

## Physical exercise interventions in cancer survivors: effects and methodological issues? – Anne May (The Netherlands)

For many patients, cancer and its treatment are associated with physical and psychosocial side-effects, including reduced physical fitness and function and increased risk of anxiety, depression and fatigue, which has a negative influence on patients' quality of life. Physical exercise interventions have the potential to beneficially affect these outcomes. Several meta-analyses have shown beneficial effects of exercise interventions on cancer patients' quality of life, fatigue, physical functioning and fitness during and after completion of treatment. Recently the Predicting OptimaL cAncer RehabIlitation and Supportive care (POLARIS*) consortium has been established: 34 exercise-oncology RCTs are pooled in one database in order to perform meta-analyses based on individual patient data. First results for quality of life will be presented.

Exercise is an intervention that cannot be blinded, which has the possible disadvantage of difficult accrual, drop-out after randomization to control, and contamination between study groups (mainly non-compliance in controls). In the second part of the presentation, the set-up of the UMBRELLA Fit study will be presented. In this study a new trial design, the cohort multiple Randomized Controlled Trial (cmRCT), is applied, which has the potential to overcome the here mentioned disadvantages. In the UMBRELLA Fitstudy the short- and long-term effects of exercise on quality of life in 166 breast cancer patients participating in the UMBRELLA cohort (University Medical Center Utrecht, NL), Utrecht) are investigated as well as feasibility of the cmRCT design in the field of exercise-oncology.

*Buffart LM et al. Predicting OptimaL cAncer RehabIlitation and Supportive care (POLARIS): rationale and design for meta-analyses of individual patient data of randomized controlled trials that evaluate the effect of physical activity and psychosocial interventions on health-related quality of life in cancer survivors. Syst Rev. 2013 Sep 13;2:75.

## Impact of weight change on cancer prognosis – Andrew Renehan (UK)

Background: Weight management is recommended after diagnosis in patients with obesity-related cancers. Rationale include that excess body weight is (i) associated with poor prognosis; (ii) increased non-cancer mortality; (iii) prevention of second primary cancers; and (iv) reduced quality of life (QoL). Here, the focus is on prognosis.

**Methods:** A critical appraisal of the evidence in the prognosis domain was performed, mainly drawing on systematic reviews (search: Pubmed since 2010) in breast, colorectal, prostate, endometrial and ovarian cancers. The findings were interpreted against criteria used by the World Cancer Research Fund (WCRF) to grade evidence, particularly evaluating for susceptibility to confounding; when fatness exposure was measured; and for specificity of association.

**Results:** There is a large volume of data, especially for breast cancer, linking elevated body mass index (BMI), measured either pre-diagnosis or < 12 months post-treatment, with increased overall mortality and reduced breast cancer-specific survival. Findings for the other cancers were mixed. There was a paucity of studies where BMI was measured during survivorship (≥ 12 months post-treatment). In many studies, the possibilities of confounding cannot be excluded – for example, many studies lacked data on stage and treatment. Except for ER+ breast tumours, few analyses demonstrated specificity of association.

**Conclusions:** Much of the evidence underpinning the rationale for weight management after cancer diagnosis is WCRF grade 'limited suggestive'. This interpretation challenges many contemporary commentaries. Long-term oncological outcomes are awaited from a small number of cancer-specific trials assessing the impact of weight management.

# SPEAKER ABSTRACTS

## Weight loss interventions in cancer survivors – Wendy Demark-Wahnefried (US)

Consensus now exists that obesity is a risk factor for nine different cancers; therefore, many cancer patients present with obesity at the time of diagnosis and often gain even more weight with various cancer therapies. Given that obesity is a poor prognostic indicator for roughly 15 different cancers and also increases the risk for common comorbidities, such as cardiovascular disease and diabetes, the American Society of Clinical Oncology (the largest organization of oncologists in the world) issued a position statement on obesity, encouraging practitioners to reinforce weight management in this patient population.

While some of the lessons learned in conducting weight loss interventions in the general population can be applied to cancer survivors, survivors have several issues (many related to cancer and its treatment) which call for modified approaches to weight management. Moreover, some of the more compelling research questions call for focused energy balance research among cancer survivors. Examples of such research questions are as follows: Will negative energy balance (either caused by caloric restriction, increased physical activity or both) result in improved cancer control, as well as other key outcomes? Does weight control exert similar effects across various neoplasms and are there optimal times to intervene? …And, what are key elements of optimal interventions in cancer survivors? Information from previous reviews and findings of more recent clinical trials will be presented to begin to answer these research questions and show where challenges and gaps remain.

## The impact of obesity on cancer risk in low-middle-income countries – Ellen Kampman (The Netherlands)

The obesity epidemic is growing faster in low-middle-income countries (LMICs) than in high-income countries (HICs). The rapid increase in BMI in LMICs is associated with urbanization, economic development, changes towards a 'Westernized' diet and lower physical activity.

The increasing prevalence of overweight and obesity appears to have a substantial contribution to cancer burden in LMICs. Although awareness of the importance of cancer in LMICs is increasing, there is still the misperception that infectious diseases represent the primary health issue in LMICs, and that cancer risk is not preventable or modifiable, and is not related to nutrition and physical activity.

To date, most evidence linking overweight/obesity to cancer comes from HICs, where the combination of risk factors and exposures may differ from those in LMICs. Many LMICs now face a double burden where rates of overweight and obesity are increasing, while undernutrition persists. A major challenge is to capture and better understand the interplay between early-life and current dietary exposures that can alter infants' and children's growth patterns, metabolism, risk of obesity and cancer in adulthood. Population surveys, etiologic and intervention studies, as well as implementation research are important in developing the evidence base to tackle the rise in cancers associated with obesity. Future studies should take local determinants, differences in tumor biology, subtypes, and genetic variants into account. High priority is to build capacity in LMICs to undertake high quality research and to provide high quality information supporting government policy and action plans increasing awareness.

## IARC Handbook – Weight management and cancer prevention – Rudolf Kaaks (Germany)

In 1995, the IARC Handbooks of Cancer Prevention were launched to complement the IARC Monographs' evaluations of carcinogenic hazards with evaluations on the scientific evidence on preventive agents and primary and secondary interventions. The working procedures and the evaluation scheme of the IARC Handbooks of Cancer Prevention closely mirror those of the IARC Monographs. Interdisciplinary working groups of expert scientists review the published studies and evaluate the weight of the evidence that an agent or activity can act as cancer-preventive.

In 2002, a first working group to assess the preventive effects of weight control on cancer risk concluded that there was sufficient evidence in humans for a cancer-preventive effect of avoidance of weight gain for cancers of the colon, esophagus (adenocarcinoma), kidney (renal cell), breast (postmenopausal), and corpus uteri. In April 2016, based on the review of more than 1000 epidemiological studies on cancer risk and excess body fatness, a new working group reaffirmed that absence of excess body fatness lowers cancer risk at the sites previously identified, and additionally identified eight further cancers (gastric cardia, liver, gall bladder, pancreas, ovary, and thyroid, multiple myeloma, meningioma) for which there is now also sufficient evidence that absence of body fatness lowers cancer risk. For cancer of the breast, endometrium and ovary, the association with excess body fatness was reduced or absent among women using postmenopausal hormone replacement therapy.

In addition to the cancer sites for which there was sufficient evidence, the working group concluded that there is limited evidence for an association between excess body fatness and fatal prostate cancer, diffuse large B-cell lymphoma, and male breast cancer. For eight other cancers (lung, esophagus [squamous cell carcinoma], gastric non-cardia, extra-hepatic biliary tract, skin [cutaneous melanoma], testis, urinary bladder, and glioma) the evidence for an association was considered inadequate, due to limited data, inconsistent results, or no data suggesting an association.

Experimental animal studies confirmed that obesity in rodents promotes tumorigenesis and increases the incidence of cancers of the mammary gland, colon, liver, pancreas, prostate (advanced stage), and skin, and to a lesser extent, leukemia. Furthermore, a large number of studies in rodent models showed evidence for a cancer-preventive effect of limitation of body-weight gain by caloric/dietary restriction, for cancers of the mammary gland, colon, liver, pancreas, skin, and pituitary gland, whereas an inverse association was observed between caloric or dietary restriction and cancer of the prostate, lymphoma and leukemia. Regarding mechanisms, the working group identified strong evidence for obesity-related alterations in sex hormone metabolism chronic inflammation in mediating the obesity-cancer relation, and moderate evidence for a role of insulin/insulin-like growth factor signaling.

Studies on the effects of controlled weight-loss were sparse. Nonetheless, data on body-weight loss, either from observational studies or from follow-up of patients undergoing bariatric surgery, did suggest that intentional weight loss may reduce cancer risk, notably for breast and endometrial cancer, although the number and quality of these studies was judged insufficient for a formal evaluation.

## Increasing Public Acceptability of Policies tackling Obesity – Theresa Marteau (UK)

The causes of obesity are complex but overconsumption of food and sugary drinks is a critical proximal determinant. Evidence is accumulating to show the potential effectiveness of Choice Architecture interventions (Nudging) such as reducing size and availability of less healthy products, and price-based interventions such as increasing the price of sugary drinks. Many of these interventions will require regulation for which public acceptability will be a critical consideration for policy-makers.

Paradoxically, public acceptability is high for the least effective interventions, which are information-based, and lower for Choice Architecture and price-based interventions, which are more effective.

This presentation will outline a possible resolution to this paradox arising from findings from several studies showing that public perception of intervention effectiveness is one of the most reliable predictors of intervention acceptability. This leads to the testable hypothesis that presenting evidence of an intervention's effectiveness at changing behaviour to tackle obesity increases its acceptability to the public, and in turn, policy-makers.

## Implementing science into actions for obesity prevention – Juan Rivera (Mexico)

México is facing an obesity epidemic with prevalences of excess BMI (overweight and obesity) of 70% in adults and about 33% in school-age children and adolescents. The National Public Health Institute in Mexico (HPHI) has generated a body of scientific evidence aimed at supporting the design of policy for its prevention and control. Monitoring though periodic National Health and Nutrition Surveys (NHNS) since 1988 provided information about the magnitude, distribution and trends of excess BMI during the last three decades. In less than a quarter of a century obesity in adult women increased from 9.5% to 35.2%. This dramatic rise alerted the government about the urgent need for interventions. The NPHI has conducted the following set of studies aimed at generating information to inform policymaking: a) Monitoring changes in key drivers of obesity through NHNS have been useful to identify shifts in the diet that may be responsible for the increase of obesity. b) Formative research allowed recognition of obesogenic elements in different environments and barriers for the adoption of healthy eating and physical activity. c) Randomized efficacy trials have tested effects of specific interventions. D) Estimation of own- and cross- price elasticities of SSB provided justification for a tax on these products. E) the evaluation of policy actions has provided feedback for redesign or improvements. The evidence from these studies led to recommend a comprehensive strategy for the prevention of obesity, which started in 2010 and we are currently evaluating.

## Facilitating the uptake of policies to promote healthy lifestyles and estimating their impact – Linda Bauld (UK)

More than four in ten cancers in the United Kingdom could be prevented by modifying behavioural risk factors, a pattern that is also observed in other countries. Using the UK as an example, this presentation will examine the relationship between overweight and obesity and cancer risk and outline how policy interventions could reduce the number of obesity-related cancers, particularly if the actions taken affect children and families.

Evidence strongly suggests that children with excess bodyweight are more likely to become overweight or obese as adults, increasing their risk of at least ten types of cancer. In the UK, one in five children are overweight or obese when they enter primary school and by age 11, this rises to one in three. If these rates continue, almost three in four adults could be overweight or obese by 2035.

# SPEAKER ABSTRACTS

Individual behavioural interventions have a role to play, but the most significant gains are likely to be made at the population level if policies are introduced that address some of the main drivers. These include price, promotion, the product and place-based measures. Working with the Obesity Health Alliance, a multi-agency national partnership, CRUK has recently invested in research that makes the case for policy change on both price and promotion. This presentation will focus in particular on the changes needs to address the promotion of foods high in salt, sugar and fat to children in the UK and how these types of marketing restrictions are likely to contribute to cancer prevention in the future.

## How to balance policies for the prevention of obesity, cancer and other NCDs – Alan Jackson (UK)

Obesity represents the progressive accumulation of excessive fat mass over extended periods of time which is both a cause and a consequence of disordered integrated metabolism, which can lead to the related pathologies and co-morbidities identified as chronic non-communicable diseases. In practice it is marked as an unusually high body mass index, or great than usual waist circumference. Achieving a reduction in fat mass leads to a reduction in risk and clinical improvement for established disease. In contrast, achieved adult height or height at earlier ages is differentially associated with greater risk for cancer, but lesser risk for heart disease and type 2 diabetes. The basis for this difference in risk between cancer and other conditions is not known. Interventions to modulate either the rate of height gain or height loss are difficult to impossible. Stunting, or linear growth impairment during early life and childhood is associated with significantly reduced cognitive and physical development, themselves causally related to constrained lifetime opportunities. For these reasons the correction of stunting is an important priority for the global health agenda, as captured within the Sustainable Development Goals. The underlying biology relating height to risk of cancer on the one hand and protection from cardiovascular disease or type 2 diabetes, on the other hand, is unclear. Mechanistic biology at the different levels of organisation: molecular, cellular, tissue and whole body needs to place priority on providing explanations for these epidemiological observations so that effective policies can be developed that do not increase the risk of cancer while reducing the risk for other diseases.

## Cancer and Nutrition NIHR infrastructure collaboration: future research directions – Alan Jackson (UK)

The Cancer and Nutrition NIHR infrastructure collaboration was established in early 2014 against the need to better align research activities. The UK has world leading research both in cancer and in nutrition but historically the research in the two areas has not been brought together sufficiently to make full use of the potential opportunities.

Cancer patients want guidance on how to achieve the best quality of life, to slow the development or progression of their cancer, and to improve their survival. Unfortunately the lack of reliable evidence often means that health professionals are not able to provide evidence-informed advice, and hence patients find unreliable information from unaccredited sources. Clinicians need evidence to make informed decisions and advise patients appropriately. However, they have told us that the lack of reliable evidence on how nutrition and related factors affect those living with cancer makes giving such advice problematic. Patients, charities, researchers and clinicians have a key role to play in enabling and supporting the generation of evidence that both patients and healthcare professionals need, and are asking for, to ensure cancer patients get the best possible care.

To bridge this gap the Collaboration has developed five work streams to better enable collaborative and mutually supportive endeavours (http://cancerandnutrition.nihr.ac.uk/).

# ORAL PRESENTATION ABSTRACTS

## DAY 1

### The effects of caloric restriction on molecular mechanisms related to tumorigenesis in the colon of C57BL/6J mice.

Dieuwertje Kok[1], Fenni Rusli[1], Carolien Lute[1], Ellen Kampman[1], Michael Müller[2], Wilma Steegenga[1]

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Obesity is linked to an increased risk of multiple types of cancer, including colon cancer. From this perspective, caloric restriction (CR) has been considered a strategy to restore the energy balance and prevent tumorigenesis, although the underlying mechanisms are poorly understood. The aim of this study was to provide a comprehensive overview of the impact of CR on colonic health.

Male C57BL/6J mice received a life-long CR diet with 30% energy reduction, or a control (C) diet or medium-fat (MF) diet ad libitum. Mice (n=8-18/group) were sacrificed at the age of 6 or 28 months and colon, blood and urine samples were collected. Colonic gene expression profiles, levels of short chain fatty acids, microbiota composition, serum cytokine levels and urinary metabolites were determined.

After CR, expression of genes related to inflammatory and immune response pathways was down-regulated compared to the C/MF diet. Also serum levels of the pro-inflammatory cytokine interleukin 6 were lower in mice on CR as compared to the MF diet ($p<0.05$). Microbial profiling showed that CR resulted in a higher abundance of the **Bifidobacterium** and **Lactobacillus** genera, whereas **Clostridium sensu stricto 1** was less abundant compared to the other diet groups. Furthermore, microbial richness was correlated with body weight at sacrifice ($r=0.613$, $p<0.001$).

These findings indicate that prolonged CR is associated with complex and integrated molecular phenomena related to metabolic, anti-inflammatory and immune responses. Detailed insight into effects of CR may facilitate development of feasible strategies to reduce energy intake and thereby prevent obesity and cancer.

### The Novel Adipokine Omentin, Obesity and Colorectal Cancer: New Insights from the EPIC - Potsdam Cohort Study

Krasimira Aleksandrova[1], Romina di Giuseppe[2], Berend Isermann[3], Ronald Biemann[3], Matthias Schulze[4,5,6], Clemens Wittenbecher[4,5], Andreas Fritsche[5,7], Rainer Lehmann[5,7], Juliane Menzel[4,5,8,9], Cornelia Weikert[6,8,9,10], Tobias Pischon[11], Heiner Boeing[12]

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Omentin is a novel pleiotropic adipokine linked to obesity, immune response and metabolic dysfunction; thereby it could play a role in the development of colorectal cancer (CRC). However, the association between omentin and CRC risk has not been evaluated in prospective cohort studies. We explored the association between circulating plasma omentin concentrations and risk of CRC in a case-cohort study comprising 251 incident CRC cases diagnosed over a mean follow-up time of 10.4 years and 2,295 persons who remained free of cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC)-Potsdam. Hazard ratios as a measure of relative risk (RR) and 95% confidence intervals (CI-s) were computed using a Prentice modified Cox regression. In a multivariable model adjusted for age, sex, education, dietary and lifestyle factors, body mass index (BMI) and waist circumference, higher omentin concentrations were associated with a higher CRC risk ($RR_{\text{continuously per doubling of omentin concentrations}}$=1.98, 95% CI: 1.45-2.73). Additional adjustment for metabolic biomarkers, including glycated hemoglobin, high-density lipoprotein cholesterol and C-reactive protein, did not alter the results. In stratified analyses, the positive association between omentin and CRC risk was observed in participants with BMI < 30 (RR=2.26; 95% CI: 1.57-3.27), whereas among participants with BMI ≥ 30 no association was revealed (RR = 1.07; 95%CI: 0.63-1.83; $P_{\text{interaction}}$ = 0.005). These data suggest for the first time an independent association between circulating omentin concentrations and CRC risk. Furthermore, the data revealed a potential interaction with the adiposity state of an individual that requires further evaluation in future research.

# ORAL PRESENTATION ABSTRACTS

## DAY 1

### A study on effect modification by mTOR/PI3K/Akt gene variants of associations between body size, physical activity, early life energy restriction and colorectal cancer risk

Colinda C.J.M. Simons[1], Leo J. Schouten[1], Roger W.L. Godschalk[2], Frederik-Jan van Schooten[2], Monika Stoll[3, 4], Kristel van Steen[5], Piet A. van den Brandt[1], Matty P. Weijenberg[1]

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**Introduction:** The influence of body size, physical activity and early life energy restriction on colorectal cancer (CRC) risk may be modified by mTOR-PI3K-Akt gene variants. These genes integrate signals from nutrients and growth factors and affect (cancer) growth.

**Methods:** The Netherlands Cohort Study includes 120,852 men and women. Participants were 55–69 years old and self-administered a questionnaire in 1986. Follow-up was 20.3 years. In toenail DNA, we genotyped 18 tagging variants in top mTOR genes according to the relative betweenness centrality measure (**MTOR, TSC2, PDK1, EIF4EBP1, RPS6KB2, AKT3, AKT2**), GWAS hits for body size in the mTOR pathway, and a cancer risk-increasing mTOR variant from a meta-analysis. Sex-specific hazard ratios and 95% confidence intervals for CRC were estimated by Cox regression comparing genotypes and exposure variables within genotype strata (case-cohort approach: n subcohort = 3,550; n cases = 3,293).

**Results:** Several variants in **MTOR, RPS6KB2, AKT3, RPTOR** and **INSR** were associated with CRC risk, but not after adjustment for multiple testing. There was a diverging risk pattern across genotype strata (dominant model) for body mass index (BMI), height, and early life energy restriction, but not waist circumference, physical activity and BMI at age 20, in relation to CRC risk in men and women. The pattern was also present for the proximal colon and rectum, but not the distal colon. Interactions were nonsignificant (P>0.05).

**Conclusion:** There was no clear evidence that **mTOR-PI3K-Akt** gene variants modified associations between body size, physical activity and early life energy restriction and CRC risk.

### Energy balance-related factors and breast cancer risk in pre- and post-menopausal women

Doris S.M. Chan[1], Snieguole Vingeliene[1], Dagfinn Aune[1,2], Elli Polemiti[1], Leila Abar[1], Rita Vieira[1], Darren C. Greenwood[3], Teresa Norat[1]

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**Aim:** To systematically review the findings from prospective studies of energy balance-related factors (physical activity, obesity, and adult weight gain) and breast cancer (BC) risk in pre- and post-menopausal women.

**Methods:** Relevant publications on the associations of interest were searched in PubMed up to April 2015, (part of the World Cancer Research Fund Continuous Update Project). Random-effects meta-analyses were conducted to calculate the summary relative risks (RRs) for pre- and post-menopausal BC.

**Results:** Early adulthood (age 18–<30 years) body mass index (BMI) was significantly inversely associated with pre- and post-menopausal BC (summary RRs per 5 kg/m$^2$=0.82, 95% confidence interval (CI)=0.76–0.89 and 0.82 (0.76–0.88), respectively). Adult weight gain significantly increased the risk of post-menopausal BC but not pre-menopausal BC (summary RRs per 5 kg gain=1.06, 95% CI=1.05–1.08 and 0.99 (0.96–1.03), respectively).

In pre-menopausal women, greater BMI and higher vigorous physical activity was significantly inversely associated with BC risk; when BMI was accounted for in the studies, increased risk was observed with greater waist circumference (WC) (summary RR per 10 cm=1.14, 95% CI=1.04–1.26) and similarly with waist-hip-ratio (WHR).

BC risk in post-menopausal women was consistently elevated with higher BMI, WC, and WHR (adjusted or not adjusted for BMI) and reduced with higher physical activity. For each 10 metabolic equivalent of task-hour of recreational physical activity/week, post-menopausal BC risk was reduced modestly but significantly by 2% (95% CI=1%–3%).

**Conclusions:** Greater abdominal obesity (WC/WHR) throughout life increases pre- and post-menopausal BC risk. After menopause, the effect of excessive general obesity (BMI) is more relevant.



# ORAL PRESENTATION ABSTRACTS

## DAY 2

### Body mass index and renal cell cancer: associations with tumour characteristics and overall survival

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**Introduction:** Overweight is an important risk factor for developing renal cell cancer (RCC). In contrast, RCC patients who are overweight or obese at diagnosis appear to have more favourable disease characteristics and better survival than patients with a normal body mass index (BMI). Disease-related weight loss may partly explain these findings. The objective of this study was to assess the association of average BMI during adult life with tumour characteristics and with overall survival in RCC patients.

**Methods:** Patients diagnosed with RCC between 1989-2008 in eight hospitals in the Netherlands were identified through the Netherlands Cancer Registry (NCR). Self-reported average BMI during adult life was obtained by postal lifestyle questionnaire at study inclusion in 2009. Logistic regression analysis and delayed entry multivariable Cox regression analysis were used to assess the association of BMI with tumour characteristics and with overall survival, respectively.

**Results:** A total of 426 RCC patients were eligible for analysis and 103 of them died. No association of overweight and obesity with tumour stage and with overall survival was found (overweight: HR=0.93; 95% confidence interval [CI], 0.59-1.46 and obesity: HR=1.63, 95%CI, 0.92-2.88, respectively). In 217 RCC patients with information on Fuhrman grade, those who were overweight or obese were more likely to be diagnosed with lower Fuhrman grade (3+4 vs. 1+2: odds ratio [OR]=0.49; 95%CI, 0.24-0.99 and OR=0.14, 95%CI, 0.03-0.62, respectively, p-trend<0.01).

**Conclusion:** Overweight or obesity during adult life were associated with lower Fuhrman grade at diagnosis but no associations with tumour stage and overall survival were found.

### Lifecourse evolution of body shape and survival after breast cancer in the French EPIC-E3N cohort study

Mathilde His[1,2], Marine Le Guélennec[1,2], Sylvie Mesrine[1,2], Marie-Christine Boutron-Ruault[1,2], Françoise Clavel-Chapelon[1,2], Guy Fagherazzi[1,2], Laure Dossus[3]

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**Background:** Although weight changes around breast cancer diagnosis have been extensively studied in relation with survival, few studies have explored lifecourse evolution of excess fat mass before diagnosis in relation to breast cancer prognosis. We investigated the relationship between body shape at different ages in life and body shape trajectories, and breast cancer survival.

**Methods:** Analyses included 4,563 women from the French E3N prospective cohort study diagnosed with primary invasive breast cancer between 1990 and 2008. We considered Sørensen's body shapes at 8, menarche, 20-25 and 35-40 years (8 shapes, leanest to largest) in relation to survival (overall, breast cancer-specific, and disease-free), overall and according to stage, menopausal and hormone receptor status, and year of diagnosis. We used Cox proportional hazard models adjusted for tumour characteristics and lifestyle risk factors. We will next investigate lifetime body shape trajectories using Nagin's approach of group-based trajectory modelling, in relation to breast cancer prognosis.

**Results:** Mean pre-diagnostic BMI of women from our study population was 23.6 kg/m$^2$. Compared with the leanest women (body shape 1), women with a larger body shape at menarche (body shapes 4 to 8) had a decreased risk of recurrence or death: HR=0.83, CI=0.69-0.99, even after adjusting for pre-diagnosis BMI (HR=0.81, CI=0.68-0.98). Subgroup and trajectory analyses will be performed, and results will be presented at the conference.

**Conclusions:** These preliminary results suggest that adiposity early in life influences prognosis of breast cancer. Further analyses will help understand key periods and breast cancer subtypes involved in these relationships.

### Serum glucose, triglycerides and cholesterol and prostate cancer survival

R. Arthur[1], H. Møller[1], H. Garmo[1,2], C. Häggström[4], L. Holmberg[1,2,3], P. Stattin[3,4], H. Malmstrom[5], M. Lambe[3,6], N. Hammar[5,7], G. Walldius[8], D. Robinson[4], I. Jungner[9], M. Van Hemelrijck[1,5].

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**Background:** Obesity has been associated with prostate cancer (PCa) progression, but the link with other obesity-related disorders including hyperglycemia and dyslipidemia is unclear.

# ORAL PRESENTATION ABSTRACTS

Here, we assessed the association between levels of serum glucose, cholesterol, and triglycerides and PCa deaths.

**Methods and material:** From the Swedish AMORIS cohort, we selected all men diagnosed with PCa between 1996 and 2011 who had baseline measurements of serum glucose, triglycerides and total cholesterol and whose tumour information (i.e. TNM stage, Gleason score, and PSA) was registered in the National Prostate Cancer Register (n=14,150). In addition, we used information on sociodemographic characteristics, comorbidities and cause of death. Multivariable Cox proportional models were used to determine the hazard ratios (HR) for PCa-specific and all-cause mortality by quartiles of glucose, triglycerides and total cholesterol.

**Results:** Glucose had an independent positive association with all-cause mortality (HR for highest versus lowest quartile: 1.18; 95% CI: 1.07-1.31). Similarly, risk of PCa deaths increased with increasing glucose levels (HR: 1.20; 95% CI: 1.03-1.39). Risk of death from all-causes was higher among hypertriglyceridemic men than those with normal triglycerides levels (HR: 1.14; 95% CI: 1.03-1.26 and 1.16 (1.05-1.30) for third and fourth quartiles versus first), but PCa-specific death rates did not vary. Survival did not differ by total cholesterol levels.

**Conclusion:** Our results suggest that glucose metabolism influences PCa survival. However, more research on the link between glucose and PCa survival is needed to validate our findings as management of glucose levels may have therapeutic importance in helping to control PCa progression.

## Randomised controlled trial of continuous versus intermittent energy restriction during adjuvant chemotherapy (The B-AHEAD2 Trial)

Michelle Harvie[1], Mary Pegington[1], Anne Armstrong[2], Nigel Bundred[1], Julie Morris[3], Judith Adams[4], Lee Graves[5], Louise Gorman[1], Alastair Greystoke[6], Sacha Howell[1,2], Anthony Howell[1,2]

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**Background** Observational data indicate that excess weight at breast cancer diagnosis and weight gain during adjuvant chemotherapy increases risk of recurrence and death. We have reported that continuous energy restriction (CER) and exercise is only partially effective for weight control during chemotherapy. Randomised trials in healthy subjects indicate that intermittent energy restriction (IER) may be equivalent or superior to CER for weight control, and animal data suggest reduced chemotherapy toxicity with IER. Here we will report the results of a randomised comparison of IER vs. CER amongst 172 women receiving adjuvant /neoadjuvant chemotherapy.

**Methods:** Women were recruited immediately after surgery. IER (n = 86) or CER (n = 86) was administered throughout the 4.5–6 month course of chemotherapy The primary end point was body weight, body fat & lean body mass assessed with DXA. Secondary endpoints were chemotherapy toxicity (self-report CTCAE and Cytokeratin 18 and FMS like Tyrosine Kinase 3 ligand serum markers), quality of life (FACT scales) and serum markers associated with prognosis (insulin sensitivity, adiponectin, leptin).

**Results** Uptake was 39%. Twenty eight women (16%) failed to complete the study; 19 IER and 9 CER. High uptake and adherence reflects interest and motivation of women to make positive changes to lifestyle even at the time of diagnosis.

**Conclusion** Results are currently being analysed. We will report changes in body weight composition and toxicity, and serum markers associated with prognosis between IER and CER at the September.



# POSTER PRESENTATIONS

The poster abstracts are ordered by alphabetical order of first author. The presented posters will be displayed in the exhibition and refreshment area.

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| 3 | Physical exercise in newly diagnosed breast cancer patients may counteract a decrease in cardiovascular capacity during adjuvant treatment | Anders Husøy |
| 4 | Physical Activity during Cancer Treatment (PACT) study: randomized clinical trial of physical exercise during cancer treatment – long-term effects on physical activity levels | Anouk Hiensch |
| 5 | Inflammation and breast cancer risk: a case-control study nested in the EPIC-Varese cohort | Claudia Agnoli |
| 7 | Body mass index and cancer risk: a systematic review and dose-response meta-analysis of cohort studies. | Dagfinn Aune |
| 10 | Applying computed tomography-based body composition analysis to assess adipose and muscle tissue parameters at colorectal cancer diagnosis and investigate associations with long-term health-related quality of life | Eline van Roekel |
| 11 | ReStOre - Rehabilitation Strategies following Oesophageal Cancer: The impact of a multimodal rehabilitation programme on inflammatory status and oxidative stress. A Feasibility Study | Emer Guinan |
| 12 | Lifestyle related health factors after cancer treatment | G. Haukur Guðmundsson |
| 13 | Irregular intake of energy and alcohol is not associated with an increased risk of breast cancer in UK women | Gerda Pot |
| 14 | Physical activity and quality of life in men living with advanced prostate cancer | Grainne Sheill |
| 15 | Disturbed NK cell function in obesity is associated with an increased colon tumor risk | Ina Bähr |
| 16 | Inflammatory Potential of Diet and the Risk of Colorectal Tumours in Persons with Lynch Syndrome | Jesca GM Brouwer |
| 17 | Perceived facilitators and barriers to a physical exercise programme in oesophageal cancer patients after surgery | Jonna K. van Vulpen |
| 18 | Colorectal cancer survivors' adherence to the cancer prevention recommendations of the WCRF/AICR and cross-sectional associations with health-related quality of life | Jose J.L. Breedveld-Peters |
| 19 | Natural killer cell functionality is impaired by diet-induced obesity in a postmenopausal breast cancer mouse model | Julia Spielmann |
| 21b | Mediating factors of the association between adult weight gain and colorectal cancer: Data from the European Prospective Investigation into Cancer and Nutrition (EPIC) Cohort | Krasimira Aleksandrova |
| 22 | The Impact of a Structured Exercise Programme on Adipokine Status in Patients with Metastatic Prostate Cancer | Lauren Brady |
| 23 | Anthropometric factors and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies | Leila Abar |
| 24 | Survival after breast cancer among women with anorexia nervosa | Lene Mellemkjær |
| 25 | ReStOre - Rehabilitation Strategies following Oesophageal Cancer: Achieving exercise guidelines in a nutritionally vulnerable group without undesirable weight loss: A Feasibility Study | Linda O'Neill |
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# POSTER PRESENTATIONS

| ABSTRACT NUMBER | TITLE | FIRST AUTHOR |
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| 27 | Tumor expression of fatty acid synthase and its ligand in colorectal cancer and its impact on prognosis; a Systematic Review | Marie Cantwell |
| 28 | Lower handgrip strength is associated with worse quality of life and more fatigue and disability in long-term colorectal cancer survivors | Martijn Bours |
| 31 | An increase in physical activity after colorectal cancer surgery is associated with improved recovery of physical functioning | Moniek van Zutphen |
| 32 | Body mass index, total cancer incidence and colorectal cancer in young and middle-aged men and women followed over 28 years: The Tromsø Study | Oyeyemi Sunday Oluwafemi |
| 33 | A re-audit of a weight management after cancer treatment programme. | Rachel Bracegirdle |
| 36 | Physical activity level of breast cancer patients, a comparison with the Dutch female population | Roxanne Gal |
| 39 | The WCRF/AICR continuous update project: BMI and incidence of oesophageal and gastric cancer subtypes | Snieguole Vingeliene |
| 40 | Evolution of lean body mass (LBM) during palliative systemic treatment in metastatic colorectal cancer (mCRC) patients participating in the randomized phase 3 CAIRO3 study | Sophie Kurk |
| 41 | Mendelian randomization study of triglycerides, low- and high-density lipoprotein, and the statin-targeted 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) gene, in relation to cancer risk | Tanja Stocks |
| 42 | Correlations of physical activity and obesity with all cause cancer mortality | Yih Chau Soh |

Prizes will be awarded to the best poster presentation and the best oral presentation. Voting slips for the poster presentation award are included in your delegate pack.



# POSTER PRESENTATION ABSTRACTS

## Physical exercise in newly diagnosed breast cancer patients may counteract a decrease in cardiovascular capacity during adjuvant treatment.

Anders Husøy[1], Tora J Bettum[1], Hanne Frydenberg[1], Trygve Lofterød[1], Elisabeth Edvardsen[2,3], Frøydis Fjeldheim[1], Vidar G Flote1, Gro Bertheussen[4,5], Erik A Wist[1], Sigmund A Anderssen[2], Anne McTiernan[6], Inger Thune[1,2,7]

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**Background:** Adjuvant breast cancer treatment may accelerate physiologic aging, and influence cardiovascular capacity, but much remains unclear.

**Methods:** The aim was to study the feasibility of completing a 12-month exercise intervention during adjuvant breast cancer treatment, and to evaluate the effect of exercise on cardiovascular capacity. Breast cancer patients were randomized to a control group (N=28) or to a 12-month physical activity intervention (N=31) after surgery. The intervention group participated in supervised exercise 2×60 min/week, combined with at least 60 min/week of home training. The control group received standard care. Cardiorespiratory fitness ($VO_{2max}$) was assessed during cardiopulmonary exercise testing on a treadmill before surgery, at 6 months and 12 months. Intention-to-treat analysis were performed using a linear mixed model.

**Results:** The breast cancer patients had the following means at diagnosis: age 55.4 years, body mass index (BMI) 25.2 kg/m$^2$, $VO_{2max}$ of 32.4 ml·kg$^{-1}$·min$^{-1}$. After 6 months, women in the intervention group had a 0.5 ml·kg$^{-1}$·min$^{-1}$ increase in $VO_{2max,}$ while women in the control group had a 4.1 ml·kg$^{-1}$·min$^{-1}$ decline in $VO_{2max}$. These differences in cardiorespiratory fitness were observed overall (**p**<0.001), and were more pronounced among premenopausal women (**p**=0.001), and women receiving chemotherapy (**p**<0.001). Differences were less distinct at 12 months, but did not vary by body composition.

**Conclusion:** Physical exercise during adjuvant breast cancer treatment is feasible, and may reduce a decline in cardiovascular capacity, regardless of body composition, but may vary by age and type of treatment. These findings need to be replicated in larger clinical trials.

## Physical Activity during Cancer Treatment (PACT) study: randomized clinical trial of physical exercise during cancer treatment – long-term effects on physical activity levels

Anouk Hiensch[1], Miranda J Velthuis[2], Jonna K van Vulpen[1], Elsken van der Wall[3], Petra HM Peeters[1,4], Anne M May[1]

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**Background:** A recent randomized trial, the PACT study, showed beneficial effects on fatigue and physical fitness after an 18-week supervised exercise program in breast and colon cancer patients undergoing adjuvant treatment. Yet, maintaining a physically active lifestyle after cancer treatment is reported as challenging, even though it is important to preserve achieved beneficial effects. This study aims to assess long-term effects of the PACT exercise intervention on physical activity (PA).

**Methods:** 128 out of 237 breast and colon cancer patients participated in the 4-year follow-up physical activity questionnaire (SQUASH, n=70 exercise; n=58=usual care control). We investigated minutes per week moderate-to-vigorous leisure and sport PA and total moderate-to-vigorous PA, which was assessed at baseline (within 10 weeks after diagnosis), 18-week (post-intervention), and 36-week and 4-years post-baseline.

**Results:** Intention-to-treat mixed linear model analyses showed that both moderate-to-vigorous leisure and sport PA and total moderate-to-vigorous PA decreased significantly from baseline to 18-weeks in both groups (i.e. during adjuvant treatment). Four-years post-baseline, patients returned to their baseline PA levels; and moderate-to-vigorous leisure and sport PA in the intervention group was significantly higher (85 (31;140) minutes/week). Also, compared to control, patients in the intervention group reported 142 (2;282) minutes/week more total moderate-to-vigorous PA 4-years post-intervention, whereas moderate-to-vigorous leisure and sport PA did not differ (22 (44;88) minutes/week).

**Conclusions:** Breast and colon cancer patients who participated in an exercise intervention during adjuvant treatment reported higher total PA levels four years later, emphasizing the benefits of exercising during this period.

# POSTER PRESENTATION ABSTRACTS

## Inflammation and breast cancer risk: a case-control study nested in the epic-varese cohort

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Breast cancer (BC) is one of the most frequently diagnosed cancers and the leading cause of cancer death among women. Adipokines and inflammation molecules, whose production is influenced by adiposity, may be involved in breast carcinogenesis; however data from prospective studies on their associations with BC risk are not conclusive.

We investigated the association between plasma levels of C-reactive protein, TNF-α, interleukin-6, leptin, and adiponectin in a nested case-control study on women of the EPIC-Varese cohort who gave blood samples in 1992-1997. BC cases identified up to 31 December 2009 were individually matched to control subjects. Rate ratios (RRs) 95% confidence interval (CI) were estimated by conditional logistic regression controlling for BC risk factors.

After a median follow-up of 14.9 years, 351 cases of BC were identified and matched to 351 control subjects. None of the markers was significantly associated with overall BC risk. Significant interaction between menopausal status and CRP, leptin, and adiponectin levels were found. Among postmenopausal women, high CRP levels increased the risk (RR 2.32; 95%CI:1.15-4.69 for highest vs lowest tertile), whilst high adiponectin levels reduced the risk (RR 0.40; 95%CI:0.21-0.77 for highest vs lowest tertile). Among premenopausal women, high TNF-α levels increased the risk (P trend=0.012), whilst leptin reduced the risk (RR 0.41; 95%CI:0.20-0.87 for highest vs lowest tertile). Moreover, high adiponectin decreased the risk of HER2+ (RR 0.40; 95%CI:0.17-0.95 for highest vs lowest tertile), but not of HER2- disease (RR 0.92, 95%CI:0.57-1.47, P heterogeneity 0.08).

These findings suggest a role for inflammation in breast carcinogenesis.

## Body mass index and cancer risk: a systematic review and dose-response meta-analysis of cohort studies

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**Purpose:** To quantitatively summarize the dose-response association of body mass index (BMI) and cancer risk.

**Methods:** PubMed was searched for relevant cohort studies up to April 2015 as part of the WCRF Continuous Update Project. Random effects models were used to calculate summary relative risks (RRs).

**Results:** Higher BMI was significantly related to the risk of the following cancers (all summary RRs per 5 kg/m2): total cancer 1.04 (95% CI: 1.02-1.06), esophageal adenocarcinoma 1.48 (1.35-1.62), gastric cardia 1.23 (1.07-1.40), small intestine 1.10 (1.02-1.18), colon 1.07 (1.05-1.09), rectum 1.02 (1.01-1.04), gallbladder 1.25 (1.15-1.37), pancreas 1.10 (1.07-1.14), liver 1.30 (1.16-1.46), post-menopausal breast cancer 1.13 (1.10-1.16), ovary 1.07 (1.02-1.12), endometrium 1.58 (1.51-1.65), advanced/high grade prostate cancer 1.08 (1.04-1.12), kidney 1.29 (1.24-1.34), bladder 1.05 (1.01-1.09), non-Hodgkin's lymphoma 1.06 (1.03-1.09), Hodgkin's lymphoma 1.26 (1.05-1.51), multiple myeloma 1.05 (1.01-1.09), leukemia 1.09 (1.06-1.12), thyroid 1.20 (1.10-1.30) and brain 1.05 (1.01-1.10). Inverse associations were observed for pre-menopausal breast cancer 0.92 (0.88-0.96), nonadvanced prostate cancer 0.95 (0.92-0.98) and for two smoking-related cancers: esophageal squamous cell carcinoma 0.64 (0.56-0.73), and lung cancer 0.83 (0.80-0.86). In never smokers, the summary RRs were: total cancer 1.08 (1.03-1.13), oral and pharyngeal cancer 1.02 (0.88-1.19), and lung cancer 0.93 (0.84-1.03). Inverse but not significant associations were observed for oral/pharyngeal cancer 0.89 (0.77-1.03) and non-cardia gastric cancer 0.93 (0.85-1.02). BMI was not related to risk of cervical cancer 1.03 (0.95-1.10) and laryngeal cancer 0.98 (0.93-1.02).

**Conclusion:** Higher BMI was associated with increased risk of 20 of 27 types of cancer investigated.

## Applying computed tomography-based body composition analysis to assess adipose and muscle tissue parameters at colorectal cancer diagnosis and investigate associations with long-term health-related quality of life

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**Purpose:** Increased visceral adiposity (visceral obesity) and muscle wasting (sarcopenia) at colorectal cancer (CRC) diagnosis, quantified by CT image analysis, have been unfavorably associated with short-term clinical outcomes and survival, but associations with long-term health-related quality of life (HRQoL) are unknown. We studied associations of visceral adiposity, muscle fat infiltration, muscle mass and sarcopenia at CRC diagnosis with HRQoL 2-10 years post-diagnosis.

**Methods:** A cross-sectional study was conducted in 155 stage I–III CRC survivors, diagnosed at Maastricht University Medical Center+, the Netherlands (2002-2010). Diagnostic CT images at the level of the third lumbar vertebra of 104 participants were analyzed to retrospectively determine visceral adipose tissue area ($cm^2$); intramuscular adipose tissue area ($cm^2$) and mean muscle attenuation (Hounsfield units) as measures of muscle fat infiltration; and skeletal muscle index (SMI, $cm^2/m^2$) as measure of muscle mass and for determining sarcopenia.

**Results:** Participants showed a large variation in body composition parameters at CRC diagnosis with a mean visceral adipose tissue area of 136.1 $cm^2$ (standard deviation: 93.4) and SMI of 47.8 $cm^2/m^2$ (7.2); 47% were classified as viscerally obese, and 32% as sarcopenic. In confounder-adjusted linear regression models, associations of body composition parameters with long-term global HRQoL, physical, role and social functioning, disability, fatigue, and distress were non-significant, and observed mean differences were below predefined minimal important differences.

**Conclusions:** Despite being relatively common at CRC diagnosis, we found no significant associations of visceral obesity and sarcopenia with long-term HRQoL in stage I-III CRC survivors. Prospective data are needed to confirm our findings.

## ReStOre - Rehabilitation Strategies following Oesophageal Cancer: The impact of a multimodal rehabilitation programme on inflammatory status and oxidative stress. A Feasibility Study

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**Background :** Physical, nutritional and quality-of-life compromise are known sequelae of oesophageal cancer (OC) treatment. Inflammation and oxidative stress may play a role in the processes underpinning these side-effects. Exercise and diet prescription may optimise survivorship and attenuate inflammation and oxidative stress. This feasibility study examines the impact of multimodal rehabilitation on inflammation and oxidative stress following OC treatment.

**Methods :**Patients >12 months post oesophagectomy were recruited. The 12-week programme included supervised and home-based exercise, dietetic counselling to ensure energy balance and multi-disciplinary education. Baseline and post-intervention assessments examined aerobic fitness (cardiopulmonary exercise test), physical activity (accelerometry), body composition (bio-impedance analysis) and blood draws. Serum samples were assessed for a panel of inflammatory markers (interleukin (IL)-1β, tumour necrosis factor (TNF)-α, IL-6, IL-8) using multiplex inflammatory arrays. Lactate secretion, lipid peroxidation (4-HNE) and oxidative stress (8-iso-PGF2α) were measured by ELISA. Percentage change was tested using Wilcoxon Signed Rank Test. Correlation analysis was performed using Spearman's rho.

**Results :** Twelve participants (mean (standard deviation) age 64.41(1.29) years) participated. Body composition was maintained throughout the intervention. At baseline, inflammatory status correlated inversely with sedentary behaviour (IL-6 rho=-0.74, IL-8 rho=-0.59, TNF-α rho=-0.69; $p<0.05$). IL-8 reduced significantly from pre- to post-intervention (percentage change -11.25%, $p=0.03$). While energy metabolism did not change, interestingly lactate concentration correlated strongly and inversely with aerobic fitness at post-intervention only (rho=-0.68, $p=0.02$).

**Conclusion:** Results suggest that multimodal rehabilitation following OC treatment reduced inflammatory status and improved lactate metabolism without compromising body composition. Examination of these findings in a larger trial will validate results.

# POSTER PRESENTATION ABSTRACTS

## Lifestyle related health factors after cancer treatment

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The aim of the study was to (A) evaluate body composition, health related quality of life (HR-QoL) and Personality D of people who had finished medical treatment because of cancer in the last 10 years and to (B) see whether fitness was correlated with body composition, HR-QoL and Personality D amongst cancer survivors who had finished their treatment.

Eighty participants aged 25 – 77 of both genders, who were in remission, answered questionnaires on HR-QoL (SF-36v2 and EQ-5D-3L), Personality D (DS[14]), general health, lifestyle and cancer treatment. Participants had their blood pressure measured, conducted the 6-minute walk test (6MWT) and had their body composition measured: body mass index (BMI), body fat percentage, waist and hip circumferences. SPSS was used for statistical analysis.

2/3 of participants had body composition over recommended values. Over half of the participants were overweight or obese. 66.3% had waist circumference over recommended values and 45.0% had waist/hip ratio over recommend values. Significant correlation ($p<0.05$) was found between 6MWT and body composition as well as most categories of HR-QoL. Increased fitness correlated with better body composition and higher HR-QoL. Only 13.8% of participants measured with distressed personality according to DS14.

Fitness evaluated with 6MWT seems to be able to indicate HR-QoL and body composition and therefore its use in clinical setting is supported.

## Irregular intake of energy and alcohol is not associated with an increased risk of breast cancer in UK women

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**Background:** Irregular eating could be a potential risk factor for breast cancer; however, research on this topic is scarce.

**Objective:** To study associations of irregular intake of energy and alcohol in relation to breast cancer risk.

**Design:** This case-control study included dietary intake data from 7-day estimated diet diaries of 629 UK women with breast cancer and 1,798 controls. Intakes of energy and alcohol during breakfast, lunch, dinner, and between meals were analysed using a score for irregularity based on the deviation from the 7 day mean. Conditional logistic regression models were used to estimate odds ratios (ORs) for associations between meal regularity scores across tertiles and breast cancer risk adjusting for relevant covariates. A separate model was run for post-menopausal women only.

**Results:** No associations between breast cancer risk and irregular intake of energy during breakfast (OR 0.93 95% CI 0.68-1.29, p trend 0.88), lunch (OR 0.89 95% CI 0.65-1.23, p trend 0.55), evening meal (OR 1.07, 95%CI 0.79-1.45, p trend 0.49), between meals (OR 0.95, 95% CI 0.69-1.32, p trend 0.92), and daily total (OR 0.92, 95% CI 0.65-1.96, p trend 0.51) were observed. Daily irregular intake of alcohol was also not associated with an increased risk of breast cancer (OR 1.11, 95% CI 0.79-1.55, p trend 0.57).

**Conclusions:** Irregular intakes of energy and alcohol were not associated with an increased breast cancer risk in women in this UK case-control study. Further research is required to investigate whether irregular meal patterns are associated with other types of cancer.

## Physical activity and quality of life in men living with advanced prostate cancer

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**Background:** Patients with metastatic prostate cancer live with a considerable disease burden that may have a profound impact on everyday physical function and quality of life. Little is known about physical activity levels and other lifestyle factors of patients with advanced prostate cancer.

**Methods:** ExPeCT (Exercise, Prostate Cancer and Circulating Tumour Cells), is a multi-centre clinical trial for patients with metastatic prostate cancer. Questionnaires examining quality of life (FACT-P), sleep (Pittsburgh Sleep Index), depression (PHQ-9) and physical activity (Harvard Health Professionals Study Questionnaire) are completed at baseline, three and six months.

**Result:** An interim analysis of the baseline outcome measures of 25 patients (mean age 71.62 (SD 8.08) years) was completed. Mean BMI was 29.4 (SD 7.7) kg/m2. The majority (76% (n=19)) of participants had sleep scores indicative of poor sleep quality. Sleep scores correlated negatively with global quality of life ($r=-0.54$, $p=0.009$). Patients scored lowest in the 'functional' and 'additional prostate cancer related concerns' domains of quality of life. Preliminary data demonstrate that 32% (n=8) of participants failed to reach a threshold physical activity of 9 MET h/wk, previously associated with reductions in all-cause mortality in this population. Physical activity levels were not associated with quality of life ($p=0.98$), sleep ($p=0.42$) or depression ($p=0.10$) scores.

**Discussion:** Findings highlight the association between poor quality of life and sleep in this population. In addition, initial data suggest a high prevalence of suboptimal physical activity levels among older men. Lifestyle interventions involving exercise may provide a potential mechanism to increase physical activity levels in patients with metastatic disease.

## Disturbed NK cell function in obesity is associated with an increased colon tumor risk

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**Background:** Natural killer (NK) immune cells control tumor progression and metastases. Previous studies showed altered NK cell functions in obese individuals. Obesity is associated with a higher colon cancer incidence, but underlying mechanisms remained unclear. We investigated the impact of an altered NK cell functionality on the increased colon cancer risk in obesity.

**Methods:** The cytotoxicity of leptin-incubated NK cells against colon tumor cells was determined using Europium release assay. Cytokine secretion of NK cells was measured by luminex immunoassay. Moreover, in vivo experiments in normal weight and obese rats were performed. Colon cancer growth was induced in half of the animals by injection of azoxymethane (AOM). Body weight and visceral fat mass were determined, colon tumors were characterized and tumor, splenic and hepatic NK cells were analyzed by real-time RT-PCR and immunohistochemnistry.

**Results:** The cytotoxicity of NK cells against colon tumor cells was significantly reduced after leptin incubation. Additionally, the reduced NK cell cytotoxicity by leptin was associated with a decreased IFNγ secretion. In obese rats, body weight and visceral fat mass were significantly increased compared to the normal weight animals. AOM-treated obese rats showed an increased quantity, size and weight of colon tumors compared to the normal weight AOM group. Molecular and immunohistological analyses indicate tissue specific changes in NK cell numbers as well as expression levels of activating NK cell receptors in obese animals.

**Conclusion:** The results showed that the impaired NK cell function may be one cause for the elevated colon cancer risk in obesity.

# POSTER PRESENTATION ABSTRACTS

## Inflammatory Potential of Diet and the Risk of Colorectal Tumours in Persons with Lynch Syndrome

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**Background:** Persons with Lynch syndrome (LS) have a high lifetime risk of developing colorectal tumours (CRTs) due to mutations in their mismatch repair genes. An important process in the development of CRTs is inflammation, which has been shown to be modulated by diet. We aimed to investigate the association between the inflammatory potential of diet and the risk of CRTs in persons with LS.

**Methods:** We used dietary intake of 466 persons with LS from a prospective cohort study to calculate the adapted dietary inflammatory index (ADII). Cox proportional hazard models, with robust sandwich variance estimates to adjust for dependency within families, were used to calculate hazard ratios (HR) of ADII tertiles. The adjusted model included age, smoking status and sex. Stratified analyses were performed by mutated gene and non-steroidal anti-inflammatory drugs (NSAIDs) use.

**Results:** During a median person-time of 60.9 months, 198 (42.5%) participants developed CRTs. The ADII was not associated with risk of CRTs in the adjusted model (HRhighest vs. lowest tertile:1.12 [95%CI 0.77-1.62], ptrend=0.66). The adjusted hazard ratios were higher for participants with an MLH1 mutation (HRhighest vs. lowest tertile:1.68 [95%CI 0.92-3.09], ptrend=0.23) but lower among those with an MSH2 mutation (HRhighest vs. lowest tertile:1.01 [95%CI 0.60-1.70], ptrend=0.98). Stratification by NSAID use resulted in an adjusted HRhighest vs. lowest tertile of 1.30 (95%CI 0.86-1.96, ptrend=0.29) for none-users and 0.70 (95%CI 0.31-1.59, ptrend=0.37) for users (pinteraction=0.69).

**Conclusion:** The inflammatory potential of diet does not appear to be associated with the risk of CRTs in persons with LS.

## Perceived facilitators and barriers to a physical exercise programme in oesophageal cancer patients after surgery

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**Aim:** To assess perceived facilitators and barriers to a physical exercise programme in oesophageal cancer patients after surgery.

**Methods:** Semi-structured interviews were conducted with oesophageal cancer patients (n=10*) who were randomised to the exercise group of the Physical ExeRcise Following Esophageal Cancer Treatment (PERFECT) Study. As part of this study, the patients participated in a 12-week supervised exercise programme twice weekly, and were advised to be physically active at least 30 minutes each day. Physiotherapists registered adherence (i.e., attendance at the supervised sessions) and compliance (i.e., performing the exercises according to the protocol). Transcribed interviews were analysed using a thematic content approach.

**Results:** Median adherence and compliance were high (100%, range 91.7 – 100% and 81.3%, range 71.3 – 92.6%, respectively). The most important perceived facilitators for the exercise programme were supervision by a physiotherapist, and patients' own motivation, efforts and helpful thoughts about exercise. There were only few barriers to attend and comply with the exercise programme, of which the most frequently mentioned were holidays and disease-specific barriers, such as regular endoscopic oesophageal dilation therapy and physical complaints (e.g. fatigue and gastro-oesophageal reflux), and for the home-based activities weather circumstances and conflicting activities.

**Conclusions:** Oesophageal cancer patients after surgery are well capable of performing a moderate-to-high intensity physical exercise programme. The most important perceived facilitators for the high adherence and compliance rates are supervision by a physiotherapist and patients' own motivation. Completion of the exercise programme was only minimally affected by perceived barriers such as holidays and disease-specific barriers.

## Colorectal cancers survivors' adherence to the cancer prevention recommendations of the WCRF/AICR and cross-sectional associations with health-related quality of life

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**Background:** The World Cancer Research Fund (WCRF) and American Institute for Cancer Research (AICR) lifestyle recommendations are for cancer prevention. In the absence of specific recommendations for cancer survivors, we investigated how colorectal cancer (CRC) survivors adhere to the WCRF/AICR lifestyle recommendations and how this is associated with their health-related quality of life (HRQoL).

**Methods:** The cross-sectional part of the Energy for Life after ColoRectal Cancer (EnCoRe) study includes 155 CRC survivors (stage I-III) 2-10 years post-diagnosis. Dietary intake, physical activity (PA) and body composition were measured by seven-day food diaries, the SQUASH questionnaire, accelerometery, and anthropometry. Ten recommendations were scored with 0, 0.5 or 1 point for no/low, medium, and complete recommendation adherence (overall score range: 0-10). CRC-specific HRQoL (EORTC QLQ-C30 and QLQ-CR29), disability (WHODAS), and fatigue (CIS) were assessed by self-report. The association of the overall WCRF/AICR score adherence (continuous) with HRQoL was analyzed by confounder-adjusted linear regression models.

**Results:** The mean score adherence was 4.9 (SD: 1.4, range 1.5-8.5). A higher score adherence was significantly associated with better physical functioning (ß: 2.9; 95%CI: 0.5, 5.3) and less fatigue (-3.5; -6.9,-0.1). Associations of an adherence score without the recommendations for PA attenuated the association with physical functioning but the association for fatigue was unchanged (-3.5; -7.7, 0.8).

**Discussion:** Higher adherence of CRC survivors to WCRF/AICR lifestyle recommendations for cancer prevention was associated with better physical functioning and less fatigue. The association with fatigue persisted after removing the PA sub-recommendation. Prospective studies are needed to confirm these findings.

**Keywords:** lifestyle recommendations; health related quality of life; fatigue; depression, anxiety and emotional distress; colorectal cancer survivors

## Natural killer cell functionality is impaired by diet-induced obesity in a postmenopausal breast cancer mouse model

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**Aim:** Obesity is a widespread disease and was identified as a major risk factor for malignant diseases, including postmenopausal breast cancer. Although the underlying mechanisms are poorly understood, it is known from in-vitro studies that essential functions of natural killer (NK) cells such as targeting tumor cells are disturbed in obese individuals. Thus, the aim of the present study is the investigation of NK cell functionality of obese mice in a postmenopausal breast cancer model.

**Methods:** To induce obesity, female mice (BALB/c) received either a standard chow (4% fat) or a high fat diet (34% fat) for up to 13 weeks. Thereafter, mice were ovariectomized and after 3 weeks of recovery, syngeneic 4T1-Luc2 mouse mammary tumor cells were injected orthotopically into the fat pad of the mammary gland. Twenty hours or 3 weeks after tumor cell challenging blood, tissues and tumors were collected and analyzed. Different techniques such as flow cytometry, luminex and real-time PCR aimed to analyze numbers, activity and physiological properties of NK cells.

**Results:** Body weight, visceral fat amount, plasma leptin and IL-6 levels were significantly increased in diet-induced obese BALB/c mice. Tumor burden was increased in the obese animals as compared to their lean littermates. Interestingly, the functionality of NK cells was altered in the obese mice with breast cancer.

**Conclusion:** The present study on a postmenopausal breast cancer model helps to understand basic molecular mechanisms regulating NK cell functionality in obese individuals and the association of the elevated breast cancer risk in obesity.

# POSTER PRESENTATION ABSTRACTS

## Mediating Factors of the Association between Adult Weight Gain and Colorectal Cancer: Data from the European Prospective Investigation into Cancer and Nutrition (EPIC) Cohort

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A growing body of evidence has emerged consistently suggesting that high body weight gain during adulthood is associated with a higher risk of colorectal cancer (CRC); however whether weight gain per se promotes CRC risk and what exact biological pathways may underlie this association remain unclear. A number of inflammatory and metabolic biomarkers have been suggested to play an important role in CRC carcinogenesis. We therefore evaluated the mediation effect of 20 different biomarkers on the relation between adult weight gain and colorectal cancer using data from a prospective nested case-control study among 452 incident cases diagnosed between 1992 and 2003, and matched within risk sets to 452 controls within the European Prospective Investigation into Cancer and Nutrition Cohort. The proportions of mediated effects (%) were estimated based on differences of percent effect changes in conditional logistic regression models with and without additional adjustment for individual biomarkers. Higher adult weight gain was associated with a higher risk of colon cancer [≥300 versus <300 grams per year: multivariable-adjusted relative risk =1.54; 95% confidence interval: 1.07- 2.24), but not rectal cancer (1.07; 95% confidence interval = 0.68-1.66). This association was accounted mostly for by attained waist circumference [reduction of 61%], and by selected biomarkers, including soluble leptin receptor [reduction of 43%], glycated hemoglobin [reduction of 28%] and transferrin [reduction of 17%]. These novel data suggest that the observed association between adult weight gain and colon cancer could be primarily explained by attained abdominal fatness in adult life and associated metabolic biomarkers.

## The Impact of a Structured Exercise Programme on Adipokine Status in Patients with Metastatic Prostate Cancer

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**Background:** Obesity is a global healthcare burden which is associated with lifestyle choices. Obesity, metabolic syndrome and inflammation play key roles in prostate cancer disease progression. While obesity is not predictive of prevalence, it is associated with a more aggressive metastatic disease state. We therefore sought to examine exercise as an adjunct to treatment in metastatic prostate cancer and determine its effectiveness through the assessment of obesity related markers.

**Methods:** ExPeCT (Exercise, Prostate Cancer and Circulating Tumour Cells, ICORG 15-21) is a multi-centre clinical trial for patients with metastatic prostate cancer. Participants are randomised into exercise and control arms and further stratified within groups based on clinical measurements. Patients in the exercise arm complete six months of aerobic exercise at a moderate-to-vigorous intensity. Patient serum samples were assessed for adiponectin, leptin and resistin using the Meso-Scale Discovery platform at baseline, three and six months.

**Results:** An interim analysis of eleven patients has suggested an increase in resistin levels over time in the control group compared with a decrease in the exercise group. Preliminary data from adiponectin and leptin assays demonstrated negligible changes, with adiponectin marginally decreased post-exercise. Accrual to this trial is ongoing and given the link between obesity and inflammation, a number of inflammatory mediators are undergoing investigation.

**Discussion:** Initial data suggests that resistin levels are decreased in our exercise cohort after three months. Therefore exercise may provide valuable clinical benefit to patients with metastatic disease, given the link between high levels of resistin and prostate cancer disease progression.

## Anthropometric factors and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies

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**Background:** Body mass index (BMI) is a well-known risk factor for colorectal cancer. However, the associations between abdominal fatness and adult height with colorectal cancer risk are less clear.

**Method:** We conducted a meta-analysis of prospective studies on the association between anthropometric measures and colorectal cancer risk. PubMed and several other databases were searched up to December 2015. A random effects model was used to calculate dose-response summary relative risks (RR's).

**Results:** 47 studies were included in the meta-analysis including 34 694 cases among 7 140 266 participants. The summary RR were 1.05 [95% (CI)1.03-1.07, $I^2$ =75.2%] per 5 kg/m2 increase in BMI, 1.05 [95% (CI)1.02-1.07, $I^2$ =89.7%] per 5 cm increase in height, 1.02 [95% (CI)1.01-1.02, $I^2$ =0%] per 5 kg increase in weight, 1.02 [95% (CI)1.01-1.03, $I^2$ =0%] per 10 cm increase in waist circumference, 1.02 [95% (CI)1.01-1.04, $I^2$ =16.8%] per 0.1 unit increase in waist to hip ratio. The existing evidence supports a positive association of total and abdominal body fatness, and colorectal cancer risk. Also, higher adult height is significantly associated with increased colorectal cancer risk.

Similar associations were observed for colon, proximal colon, distal colon, and rectal cancer, except for height and proximal colon cancer, and waist to hip ratio and rectal cancer, for which no significant associations were observed.

**Conclusion:** The positive association with height suggests that early life nutrition might play a role in colorectal cancer risk in adulthood. Higher total and abdominal body fatness during adulthood are risk factors of colorectal cancer.

## Survival after breast cancer among women with anorexia nervosa

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**Aim:** The hypothesis concerning dietary energy restriction and reduction of cancer risk is primarily based on animal experiments. Anorexia nervosa is an indicator of prolonged energy restriction in humans. We previously found that breast cancer incidence among anorexia nervosa patients was 39% lower than among population comparisons. We investigated overall survival after breast cancer among women with anorexia nervosa versus population comparisons.

**Methods:** Among 22,654 women with anorexia nervosa in National Hospital Registers in Sweden, Denmark and Finland during 1968-2010, we identified 76 breast cancer cases while 1,468 cases were observed in randomly selected comparisons from Population Registers. In the present analysis, survival after breast cancer among women with anorexia nervosa was compared to that of population comparisons by estimating hazard ratios (HRs) in Cox regression analyses with adjustment for age and calendar period. Further adjustment for extent of disease (local vs. non-localized) was performed in a subset of breast cancers.

**Results:** During follow-up after breast cancer, 23 women in the anorexia nervosa group died while 247 women in the comparison group died. The HR for overall death was 2.1 (95% CI = 1.4-3.2) after adjustment for age and calendar-period. When restricting to the subset with information on extent of disease and further adjusting for this variable, the HR was 2.6 (95% CI = 1.5-4.5).

**Conclusion:** Women with a prior diagnosis of anorexia nervosa have a worse survival after breast cancer than other women.

# POSTER PRESENTATION ABSTRACTS

## ReStOre - Rehabilitation Strategies following Oesophageal Cancer: Achieving exercise guidelines in a nutritionally vulnerable group without undesirable weight loss: A Feasibility Study

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**Background:** Malnutrition is a long-term side effect of oesophageal cancer (OC) treatment. Whilst exercise programmes have the potential to improve physical function, quality of life, and survival, the increase in energy expenditure as a result of exercise participation may result in undesirable weight loss if not managed correctly. This feasibility study aimed to demonstrate that OC survivors can achieve recommended levels of exercise through a structured diet and exercise programme without compromise to body composition.

**Methods:** Patients who were >12 months post OC curative treatment completion, including oesophagectomy, were recruited. The 12-week programme consisted of exercise rehabilitation, dietetic counselling to ensure adequate energy and protein intake, and multi-disciplinary education. Body composition was assessed pre- and post-intervention using bio-impedance analysis (Seca mBCA machine), key variables were weight(kg), fat mass(kg) and skeletal muscle mass(kg). Activity levels were monitored with Actigraph activity monitors.

**Results:** Twelve participants (mean, standard deviation (SD) age 61.4 (7.29) years, 8 male, BMI 24.01(5.02) kg/m2) completed the programme. Post-intervention all were achieving the recommended 150 minutes of moderate intensity exercise per week. This activity induced increase in energy expenditure was not associated with loss of weight from pre to post intervention (70.93(19.95)kg vs 70.29(19.47)kg p=0.169), or fat mass (19.48(8.40)kg vs 19.74(8.04)kg, p=0.596) or skeletal muscle mass (25.44(8.72)kg vs 24.86(8.97)kg, p=0.093).

Conclusion: Under the guidance of a physiotherapist and dietitian, survivors of OC may achieve exercise guidelines without compromise to body composition. The results of this study will be further verified in a randomised controlled trial.

## Adiposity and cancer: an umbrella review of the literature.

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**Background:** To evaluate strength and validity of the literature evidence on the associations between adiposity and risk of cancer.

**Methods:** An umbrella review of meta-analyses of observational studies investigating adiposity and cancer risk was conducted after searching in PubMed, EMBASE and the Cochrane library. The primary analysis focused on cohort studies exploring associations for continuous contrasts of adiposity. The literature evidence was graded into strong, highly suggestive, suggestive or weak categories after applying various criteria, such as the statistical significance of the random effects summary estimate and of the largest study in a meta-analysis, the number of cancer cases, between-study heterogeneity, 95% prediction intervals, small study effects, excess significance bias and sensitivity analysis with credibility ceilings.

**Findings:** A total of 157 meta-analyses were identified, which investigated associations of seven indices of adiposity with the development or death from 32 cancers. Of the 76 meta-analyses that included cohort studies and used a continuous scale to measure adiposity, only 11 (14%) associations for nine cancers demonstrated strong evidence. BMI was associated with a higher risk of developing oesophageal adenocarcinoma, colorectal cancer in men, biliary tract, pancreatic and kidney cancer and multiple myeloma. Weight gain and waist to hip circumference ratio were strongly associated with a higher risk of postmenopausal breast and endometrial cancer, respectively.

**Interpretation:** The association of adiposity with cancer risk has been extensively studied, but only associations for nine cancers were graded with strong evidence.

## Tumor expression of Fatty Acid Synthase and its Ligand in colorectal cancer and its impact on prognosis; a Systematic Review

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**Background:** Binding of fatty acid synthase (FAS), a cell surface receptor from the TNF receptor superfamily to its ligand (FASL) results in a death-inducing signalling complex which induces apoptosis. Clinical studies have demonstrated aberrant expression of FAS / FASL in colorectal cancer cells. The aim of this study was to systematically review studies published to date which have examined the association between colorectal tumor FAS and/or FASL expression and subsequent prognosis.

**Methods:** Using terms for FAS and FASL, Medline, Embase, and Web of Science databases were systematically searched from inception to September 2015 using appropriate MESH terms and keywords.

**Results:** Nine studies were identified for inclusion. The association between tumor FAS expression and prognosis was inconsistent; however the studies which suggested improved prognosis used monoclonal antibodies, had a large sample size, included a greater proportion of low grade tumours and did not include rectal samples. The association between FAS expression and prognosis may also be dependent on obesity; tumour FAS overexpression was associated with improved survival in non-obese patients, but predicted a worse outcome in moderately overweight/ obese patients. The association between tumor FASL expression and prognosis was inconsistent but in the studies which suggested a poorer prognosis, FASL expression was increased with advanced tumour stage, and was associated with an increase in tumour depth, lymph node involvement and presence of metastases.

**Discussion:** There is insufficient evidence to recommend FAS/ FASL expression as a prognostic marker in colorectal cancer patients. Additional studies which adjust or stratify by obesity status are warranted.

## Lower handgrip strength is associated with worse quality of life and more fatigue and disability in long-term colorectal cancer survivors

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**Purpose:** An unhealthy body composition may contribute to persisting treatment-related complaints and decreased quality of life (QoL) and functioning reported by many colorectal cancer (CRC) survivors. Therefore, we explored associations of body composition with QoL, fatigue and disability in CRC survivors.

**Design:** Cross-sectional study in 155 stage I–III CRC survivors, 2-10 years post-diagnosis. Body composition was assessed by anthropometric measures, including body mass index (BMI), waist circumference, waist-to-hip ratio, four-site skinfold measurements to determine body fat percentage, and maximum handgrip strength. Validated questionnaires were used to measure QoL (EORTC-QLQ C30; 100-point scale), fatigue (Checklist Individual Strength; 120-point scale), and disability (WHODAS-II; 100-point scale). Associations of anthropometric measures with QoL, fatigue and disability were analyzed by confounder-adjusted linear regression models.

**Results:** CRC survivors (38% females) were on average 70.1 (SD: 8.9) years of age, 5.7 (1.8) years since diagnosis, and 74.7% were overweight or obese (BMI ≥ 25 kg/m$^2$). Multivariable regression analyses showed that greater handgrip strength was significantly associated with better global QoL (β per 5 kg increment: 2.3; 95% CI: 0.3, 4.3) and physical functioning (2.9; 0.9, 5.0), and with less fatigue (-5.9; -8.7, -3.0) and disability (-2.5; -4.1, -0.9). Gender-stratified analyses showed similar results for handgrip strength in both men and women. Additionally, among men only, higher body fat percentage was significantly associated with worse physical functioning (β per 5% increment: -5.0; -9.1, -0.8) and more fatigue (5.9; 0.0, 11.7).

**Conclusion:** Lower handgrip strength was cross-sectionally associated with worse QoL, fatigue and disability in long-term CRC survivors.

# POSTER PRESENTATION ABSTRACTS

## An increase in physical activity after colorectal cancer surgery is associated with improved recovery of physical functioning

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**Background:** The influence of physical activity on patient-reported recovery of physical functioning after colorectal cancer (CRC) surgery is unknown. Therefore, we studied recovery of physical functioning after hospital discharge by (a) an increase in physical activity and (b) absolute activity levels before and after surgery.

**Methods:** We included 327 incident CRC patients (stages I-III) from a prospective cohort study. Patients completed questionnaires that assessed physical functioning and moderate-to-vigorous physical activity both before and after surgery. Cox regression models were used to calculate prevalence ratios (PRs) of no recovery of physical functioning. All PRs were adjusted for age, sex, physical functioning before surgery, stage of disease, stoma and body mass index.

**Results:** At six months post-diagnosis 54% of CRC patients had not recovered to pre-operative physical functioning. Patients who increased their activity with at least 60 min/week were 43% more often recovered (adjusted PR 0.57 95%CI 0.39-0.82), compared with those with stable activity levels. Higher post-surgery levels of physical activity were also positively associated with recovery (P for trend=0.01). In contrast, activity level before surgery was not associated with recovery (P for trend=0.24).

**Conclusions:** At six month post-diagnosis, about half of CRC patients had not recovered to preoperative functioning. An increase in moderate-to-vigorous physical activity after CRC surgery was associated with enhanced recovery of physical functioning. This benefit was seen regardless of physical activity level before surgery. These associations provide new leads to explore connections between physical activity and recovery from CRC surgery after discharge from the hospital.

## Body mass index, total cancer incidence and colorectal cancer in young and middle-aged men and women followed over 28 years: The Tromsø Study

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**Background:** Obesity is one of the preventable public health challenges linked to many co-morbidities. We used body mass index (BMI) as a measure of obesity, to investigate the relationship between BMI and total cancer incidence, and colorectal cancer.

**Method:** A population-based cohort study was carried out using the 3rd Tromsø survey of 1986-87, with linkage to the Norwegian Cancer Registry. The cohorts were aged 20-61 years (men) and 20-56 years (women) in 1986. 20 067 subjects (10 255 men; 9 812 women) were followed up for a mean period of 25.63 years. During the follow-up period, 3 220 incident cancers were identified with 1 794 (55.7%) in men, and 1 426 (44.3%) in women, with 399 cases of colorectal cancer (239 in men; 160 in women). We used Cox proportional hazards regression to compute the hazard ratio.

**Results:** A U-shaped relationship between BMI and total cancer incidence was observed in men, with BMI 20.0-24.9 kg/m2 having the lowest risk of cancer (BMI < 20.0 kg/m2: HR=1.38 [95% CI: 1.06 - 1.80]; BMI ≥ 30.0 kg/m2: HR=1.24 [95% CI: 1.01 - 1.52]). For women, a null relationship was observed. A positive linear relationship was found between BMI and the risk of colorectal cancer in men (BMI < 20.0 kg/m2: HR=0.65 [95% CI: 0.21 - 2.05]; BMI ≥ 30.0 kg/m2: HR=1.78 [95% CI: 1.07 - 2.94]). Essentially no relationship was seen in women.

**Conclusion:** The safest body weight in reducing cancer risks may be the "normal" weight. Public health policies aimed at reducing cancer incidents should address both ends of the BMI spectrum, especially in men.

## A re-audit of a Weight Management after Cancer Treatment Programme.

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**1.** Independent Cancer Taskforce. Achieving World Class Cancer Outcomes: A Strategy for England (2015-2020); **2.** NICE. Obesity: Identification, assessment and management of overweight and obesity in children, young people and adults (2014)

**Background:** The "Weight Management after Cancer Treatment" programme is open to overweight cancer survivors who have completed radical oncological treatment. It is a survivorship initiative involving teaching on healthy eating to support weight loss. The Cancer Strategy (2015-2020)[1] recognises the need for healthy lifestyle advice to reduce risk of recurrence.

**Aim:** Re-audit the clinical effectiveness of the weight management programme against NICE standards[2] and ascertain areas for improvement.

**Methods:** Weight measures were prospectively collected for participants attending the programme between February 2014-July 2015. Paired t-test analysis was used to determine statistical difference ($p<0.05$) between baseline and final weight measurements, after nine weeks active intervention. Data on participant satisfaction was gathered from 28 anonymous questionnaires.

**Results:** An average of 8 participants attended each programme over the data collection period, giving a total sample size of 40. Average weight loss was 3.4kg (3.7%) over 9 weeks duration of programme ($p<0.01$). 30%(n=12) of participants achieved 5%-11% clinically significant weight loss. 27.5%(n=11) of participants achieved a weight change of 3-<5% over 9 weeks. 42.5%(n=17) of participants achieved < 2% weight loss. All respondents had increased knowledge of a healthy lifestyle and 96.4% made lifestyle changes. 78.5% of respondents were 'quite' to 'very' pleased with weight loss progress.

**Conclusion:** Overall, weight loss outcomes achieved compared favourably to NICE standards[2]. The weight management after cancer treatment programme is effective in increasing knowledge and promoting healthy lifestyle changes in cancer survivors. Development of annual follow-up sessions was identified as an area for improvement.

## Height, genetic variants in the insulin-like growth factor pathway and post-menopausal breast cancer risk according to estrogen receptor status

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**Introduction:** Height is a risk factor for post-menopausal breast cancer (BC). To understand how growth is associated with BC, height and single nucleotide polymorphisms (SNPs) in insulin-like growth factor (IGF) pathway genes were investigated in relation to BC estrogen receptor (ER) subtypes.

**Methods:** Women (n=62,573) from The Netherlands Cohort Study self-reported height at baseline (aged 55-69). Follow-up was 20.3 years (case-cohort design). Twenty-four SNPs in 9 IGF pathway genes were genotyped in toenail DNA. Multivariable-adjusted hazard ratios (HR) and 95% confidence intervals (CI) were calculated for overall BC (n=2,387), ER+ (n=1,161) and ER- (n=249) subtypes (subcohort:n=1,704). Mediation by height was indicated: when additionally adjusting for height introduced a >10% change of HR. Genotype-height interactions were tested using the Wald-test.

**Results:** Height was associated with overall BC (HR per 5 cm=1.07, 95%CI=1.01-1.13), and specifically ER+BC (HR=1.09, 95%CI=1.02–1.17), but not with ER-BC (HR=1.02; 95%CI=0.90-1.15). **IRS1** rs1801278 and **ADIPOR1** rs7539542 were associated with overall BC risk (dominant model). Three SNPs were (borderline) significantly associated with ER+BC, but not with ER-BC risk (**ADIPOR1** rs7539542: HR(ER+)=0.79, 95%CI=0.67–0.92 and HR(ER-)=1.03, 95%CI=0.78-1.37; **IRS2** rs4773082: HR(ER+)=0.84, 95%CI=0.69-1.02 and HR(ER-)=1.04, 95%CI=0.71-1.52; **ADIPOR2** rs767870: HR(ER+)=1.15, 95%CI=0.97-1.36 and HR(ER-)=0.97, 95%CI=0.67-1.25). Additional adjustment for height did not alter the HRs. There were no significant height-SNP interactions.

**Conclusion:** Although height and **ADIPOR1, ADIPOR2** and **IRS2 SNPs** were specifically associated with ER+BC, suggesting a role for growth and energy metabolism in ER+BC development, the results do not support that these SNPs explain part of the height ER+BC association nor modify this association.

# POSTER PRESENTATION ABSTRACTS

## Physical activity level of breast cancer patients, a comparison with the Dutch female population

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**Background:** Observational research has shown that higher levels of physical activity (PA) are associated with improved prognosis in breast cancer patients. Hence, promotion of being physically active is important. We investigate PA levels of Dutch breast cancer patients and compare these with the general Dutch female population.

**Method:** Breast cancer patients were included when planned for radiotherapy and PA levels of an average week in the last months were measured (SQUASH questionnaire). The same questionnaire was used in the Dutch female population. Hours per week performing PA and adherence to Dutch PA guidelines were compared between patients and the Dutch female population. Standardized Incidence Ratios (SIR) were calculated for patients who meet the guidelines, with the Dutch female population as reference population.

**Results:** Breast cancer patients (N=424, mean age 58.5±10.6 years) were on average 34.4 hours per week physically active (including household activities). This was 8.7 hours per week less compared to the Dutch female population (N=3076, mean age 49.8±17.7 years; 95%CI -11.0;-6.4). No difference was found for meeting the guidelines (61.8% vs. 59.8%). The overall SIR of meeting these guidelines was 95% (95%CI 70;125). However, adherence to the guidelines was higher in younger patients (20-40 years; SIR=108%, 95%CI 49;204).

**Conclusions:** Shortly after diagnosis, breast cancer patients were less physically active compared to the Dutch female population. Although no differences were found in meeting the guidelines, younger patients more frequently reached these guidelines. Currently, analyses are repeated for six and twelve month follow-up data in a larger population of breast cancer patients.*

* Updated results will be presented at the conference.

## The WCRF/AICR continuous update project: bmi and incidence of oesophageal and gastric cancer subtypes

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**Aim:** To systematically review the evidence from prospective studies on the association of BMI with risk of oesophageal and stomach cancers and examine if the association differs by histological or anatomical cancer types.

**Methods:** This review has been conducted as part of the WCRF Continuous Update Project. PubMed has been searched for relevant prospective cohort studies until 28th February 2014. Random-effects dose-response meta-analyses were conducted to calculate summary relative risks (RR) for an increment of 5 kg/m$^2$ in BMI.

**Results:** Nineteen studies (28 916 cases) were included in the dose-response meta-analysis on BMI and gastric cancer and 16 studies (10 342 cases) in the analysis of oesophageal cancer. Significantly positive association was observed for oesophageal adenocarcinoma (RR=1.48 (95% CI: 1.35-1.62, $I^2$ = 37%, $P_{het}$ = 0.13, 9 studies) and gastric cardia cancer (RR=1.23 (95% CI: 1.07-1.40, $I^2$ = 56%, $P_{het}$ =0.04, 7 studies). Significant inverse association was found for oesophageal squamous cell carcinoma (RR=0.64 (95% CI: 0.56-0.73, $I^2$ = 72%, $P_{het}$ <0.001, 8 studies). High heterogeneity for squamous cell carcinoma was not explained in stratified analysis by sex, geographic location, self-reported or measured BMI, and adjustment for smoking.

**Conclusion:** The evidence from cohort studies confirms the positive association between BMI and oesophageal adenocarcinoma and gastric cardia cancer. The inverse association with SCC may be influenced by residual confounding by smoking which is a major risk factor for SCC.

**Funding source**: This study was funded by the World Cancer Research Fund (WCRF) International (Grant number: 2007/SP01).

## Evolution of lean body mass (LBM) during palliative systemic treatment in metastatic colorectal cancer (mCRC) patients participating in the randomized phase 3 CAIRO3 study

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**Background:** Observational studies suggest that low LBM is associated with chemotherapy-related toxicity and poor survival in mCRC patients. Little is known about patterns of LBM during palliative systemic therapy. Here we use data of the CAIRO3 study* in which mCRC patients with stable disease or better after 6 cycles CAPOX-B were randomized between maintenance treatment (CAP-B) and observation. Disease progression in both groups was followed by systemic reinduction therapy (CAPOX-B or other treatment) until second disease progression. We used repeated scan data of the first 62 consecutive patients to investigate LBM during treatment.

**Methods:** 196 CT-scans of 62 patients (63.7±9.4 years, n=31 maintenance; n=31 observation) were analyzed for LBM at four occasions during palliative systemic treatment using single slice evaluation at L3. Paired-sample t-tests were conducted to assess changes over time.

**Results:** Before study-randomization during CAPOX-B induction treatment, LBM decreased significantly in all patients **(-0.7kg, 95% CI -1.2; 0.3).** After randomization, LBM increased significantly during maintenance treatment (0.8kg, 0.03; 1.7, median treatment time 8.8 months) compared to the observation arm (0.2kg, -0.4; 0.8, median observation time 4.8 months). Upon first progression, during reinduction with CAPOX-B/other treatment, LBM again decreased significantly in both groups (-1.1kg, -1.7; -0.5). Updated results will be presented at the conference.**

**Conclusion:** Our preliminary data suggests muscle loss in mCRC patients during palliative chemotherapy is reversible and depends on treatment regimen. Although studies have shown prognostic capacity for LBM, the effect of subsequent changes in LBM are unknown and may be clues for new future therapeutic interventions.

*Simkens et al. **Lancet** 2015
** Results will be updated with data of more CAIRO3 participants.

# POSTER PRESENTATION ABSTRACTS

## Mendelian randomization study of triglycerides, low- and high-density lipoprotein, and the statin-targeted 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) gene, in relation to cancer risk

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**Background:** Mendelian randomization analysis makes a strong case for causality, but it has rarely been used to study blood lipids and cancer risk.

**Methods:** We included 26,904 participants from the Malmö Diet and Cancer Study. In logistic regression analysis, we used a Mendelian randomization approach with instrumental variables comprising 26-41 single nucleotide polymorphisms (SNPs) for triglycerides, low-density lipoprotein (LDL), or high-density lipoprotein, to investigate their associations with cancer risk. We also used pleiotropy-adjusted analysis to reveal associations adjusting for SNP-effects on several lipid traits, which indicates the adjusted direction of association, but not the effect size. We also investigated cancer risk by HMGCR rs12916, which affects LDL levels and is targeted in statin treatment.

**Results:** Incident cancers were 6607 in total, 1322 prostate, 1187 breast, 591 lung, 497 colon, and 400 bladder. Triglycerides was inversely related to total cancer; odds ratio per standard deviation genetic triglyceride level was 0.91 (95% CI: 0.80-1.03, P=0.1), and the association was significant in pleiotropy-adjusted analysis (P=0.01). HMGCR rs12916 per T-allele association was 1.09 (1.01-1.18, P=0.03) for prostate cancer and 0.89 (0.82-0.96, P=0.004) for breast cancer. In pleiotropy-adjusted analyses, LDL was suggestively, inversely related to prostate cancer (P=0.09, and 0.05 for prevalent +incident cases), but was not related to breast cancer (P=0.6).

**Conclusion:** Elevated triglycerides may reduce the risk of cancer overall. Also, the LDL-lowering effect of statins may increase prostate cancer risk, but statins may decrease breast cancer risk through non-targeted pathways. Replication in other populations, and investigation of potential mechanisms, are needed.

## Correlations of Physical Activity and Obesity with All Cause Cancer Mortality

Soh, Yih Chau; Soh, Chin Yun

This is a study pooling and aggregating the dataset from the World Health Organisation and the World Bank. The study was set in the year 2010. All member countries of the World Health Organisation were included in the analysis. Missing data of these member states were imputed by Markov Chain Monte Carlo and linear regression.

There is no correlation for the proportion of physical inactivity in the countries with the all cause cancer mortality rate for both gender at -0.056 (95% confidence interval, -0.168 ~ 0.068). The correlation for male is -0.073 (95% confidence interval, -0.172 ~ 0.027) and for female is -0.007 (95% confidence interval, -0.126 ~ 0.121).

There are positive correlations of the proportion of Body Mass Index (BMI) greater than 25 among nations with all cause cancer mortality for both genders at 0.207 (95% confidence interval, 0.066 ~ 0.337). However, the correlation is stronger for male at 0.367 (95% confidence interval, 0.237 ~ 0.484) and non-significant findings for female at 0.027 (95% confidence interval, -0.102 ~ 0.149).

The pooled data on the mean BMI of all WHO member countries revealed that there was correlation of the mean BMI with all cause morality at 0.129 (95% confidence interval, 0.05 ~ 0.238). The correlation is stronger for male at 0.285 (95% confidence interval, 0.160 ~ 0.399), while for female, the correlation is not significant at -0.068 (95% confidence interval, -0.180 ~ 0.042).

From this analysis, physical inactivity may not be important for all cause cancer mortality. BMI may play important role in predicting all cause cancer mortality, especially for male. Reducing BMI by controlling calorie intake and exercise may reduce all cause cancer mortality from the population level.

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