

Hot Topic Conference: Obesity, Physical Activity and Cancer

INTRODUCTION AND CONTEXT

In April 2013, IASO and WCRF International held a conference on obesity, physical activity and cancer to bring together researchers from different disciplines in the context of the links between energy balance, obesity and physical activity, and the incidence and progression of cancer.

The key objectives were to:

1. Highlight the latest research advances in the fields of obesity, physical activity and cancer and stimulate discussion about future research directions
2. Compare and contrast mechanisms underpinning the associations between obesity, physical activity, sedentary behaviour, energy metabolism and cancer development and progression
3. Explore the impact of body fatness, physical activity and sedentary behaviour in the management and outcome of diagnosed cancer
4. Raise awareness about the value of science and research in informing policy on obesity, physical activity and cancer
5. Stimulate discussion about future research directions in this area

The ambition was to explore the associations between these factors, and the processes that underpin them, from the cellular to the whole body level, with the aspiration of developing a truly transdisciplinary approach to future work in this area.

Historically, epidemiologists, clinicians and basic scientists have not often developed joint work programmes where each is integrally informed by the other. Only by integrating knowledge from all three areas will we be able to truly understand the complex processes operating in cancer and how these manifest in different experimental settings. This conference laid the foundation for future work to help make this aspiration a concrete reality.

Finally, the conference put the biological discussions into context by exploring what policy environment would be conducive to achieving population level change to reduce obesity and increase physical activity.

OVERVIEW

- Obesity, physical inactivity and cancer are global problems, and among the top causes of premature death worldwide
- The epidemiological links between these three factors are complex and interrelated
- Identifying and understanding the relationship between obesity, physical activity and cancer helps guide policy and prevention activities
- There are limitations in terms of feasibility and interpretation in extrapolation of these relationships to relevant settings for clinical, epidemiological and basic research – but all have a role and need to be better integrated
- Increasingly cellular energetics is understood to be a central factor in the abnormal behaviour of cancer cells
- Cell and animal models have provided an understanding of key genetic and biochemical pathways through which energy flux and balance can influence cellular behaviour

Obesity, physical activity and cancer risk

- Greater levels of adiposity are clearly linked to increased risk of colorectal, postmenopausal breast, and endometrial cancers, and probably also with those of pancreas, liver, kidney and gallbladder
- Greater levels of physical activity clearly protect against postmenopausal breast cancer, independently of obesity; but the two factors also interact so that the impact may differ according to body weight
- Not only are obesity and physical activity interrelated, but they also form part of a more complex cluster of behavioural and metabolic phenotypes including diabetes and metabolic syndrome. While challenging, this offers opportunities to explore the mechanisms involved
- There is growing direct evidence that weight loss in obese people reduces cancer risk, but it is difficult to study. Effective interventions to achieve weight loss in overweight or obese people or prevent weight gain are needed
- Mechanisms underpinning the links include alterations in sex or growth hormones, or inflammation as well as site-specific mechanisms; but these need to be better delineated and linked to cellular processes
- The WCRF funded research project at Bristol University [http://www.wcrf.org/cancer_research/funded_research/researcher.php] should help to provide a more robust understanding of the published literature on the mechanistic processes that link adiposity, energy balance, physical activity and cancer (including cancer survival)

Obesity, physical activity and cancer survivors

- There is less clear evidence relating obesity and physical activity to progression of cancer in survivors – this is more difficult to study and the explanations may be biological, or through impact on therapy
- Some evidence indicates that obesity may be associated with poorer prognosis, particularly for endometrial and postmenopausal breast cancer
- Greater levels of physical activity are linked to lower mortality from breast cancer among survivors
- Associations between excess adiposity and physical activity with cancer incidence may be different to the associations with adiposity and physical activity in cancer survivors; In some cancers, there may be some protective effect of being overweight during treatment - the 'overweight paradox'
- Cancer survivors are motivated and able to make modifications in diet and physical activity to promote weight loss
- Evidence from small and short-term trials suggests that proposed biological mediators are favourably affected by weight loss or activity interventions but longer term studies in cancer patients are needed to understand mechanisms and substantiate recommendations for cancer patients
- For ongoing WCRF work in this area visit www.dietandcancerreport.org

Measurement issues

- Characterising exposure is still problematic both for adiposity and activity
- BMI is an imperfect marker of fatness but more accurate methods are less suited to large scale studies
- Characterising body composition eg distinguishing lean and fat is important but not straightforward
- Physical activity is a multidimensional exposure; recall methods are most common but liable to error, and sensitive to variation tied to other cancer risk factors among different population types

- It is important to distinguish the effects of frequency, intensity and type of activity, as well as exploring independent effects of sedentary behaviour
- Biomarkers of intermediaries between adiposity or physical activity, and cancer risk or progression are informative but need to be further developed
- The study of intra-personal variability (of either biomarkers or phenotypes eg weight changes) and cancer risk is important

Lifecourse issues

- The observation that risk of some cancers in later life is associated with birthweight and attained height strongly implicates factors operating in early life in setting susceptibility to cancer
- Epigenetic alterations to the genome during fetal and childhood development can powerfully affect expression of key genes involved in nutrient and energy partitioning and metabolism, and so also impact on cellular energy metabolism
- While increased height and greater birth weight are linked to higher risk of some cancers, they are associated with lower rates of cardiometabolic diseases and conditions
- In addition, while stunting remains a problem in developing countries, it is not straightforward to simply promote greater growth without consideration of long term possible adverse effects
- Characterisation of optimal growth trajectories requires better understanding of the mechanisms and specific exposures that impact on growth, development and maturation (eg adrenarche, menarche) and on cardiometabolic and cancer risk
- Identification of epigenetic and other biomarkers of critical early life events that impact on later disease susceptibility is important

Policy issues arising from the conference discussions

- Policy action should be informed by the best available evidence, which will clarify the relationship between obesity, physical activity and cancer, build the case for action, and guide the development of effective prevention policies
- Policies should adopt a life course approach, from pre-pregnancy/maternal health through childhood, adolescence and into adulthood, both before and after cancer
- Prevention policies should aim to reduce population-level exposure to risk factors through the creation of health-promoting environments, while treatment and policies delivered in health-care settings will need to be tailored to the needs of specific at-risk or target groups, including expectant mothers and different ethnic groups.
- Policy-makers should recognise that the lifecourse trajectory for obesity is influenced by many different factors, including the nature of exposure to risk factors at different life stages. There is a complex relationship between early-life under-nutrition, stunting, and obesity, particularly as countries undergo economic transition. Policies to prevent obesity should form part of a wider package of policies that is sensitive to, and responds to, the consequences of malnutrition in all its forms.
- A comprehensive policy approach to tackle obesity is needed, which encompasses the food environment, food system and supply chain and behaviour change communication
- Globally, different countries are at different stages of their obesity epidemic, and we are unlikely to have seen the highest levels yet in many regions. Policy-makers should anticipate an increase in obesity, but take the opportunity to introduce country-specific policies early while levels are still relatively low.
- For data on global obesity prevalence visit the IASO data portal <http://www.iaso.org/resources/obesity-data-portal/>

FUTURE RESEARCH DIRECTIONS: KEY THEMES

Characterising exposures:

- Better biomarkers of dietary intake, body composition and physical activity
- Better characterisation of the different dimensions of physical activity including intensity, type and sedentary behaviour

Characterising mechanisms

- Better understanding of mechanisms underpinning the impact of early life factors on cancer and other chronic diseases
- Better understanding of mechanisms that mediate the effects of obesity and physical activity on cancer risk in adults, and research to identify ways to interrupt those mediators.
- Use of animal models that more closely reflect the human situation, and better understanding of how to extrapolate

Characterising outcomes

- Need to develop markers of disease risk, understand the time period to intervene and conduct targeted interventions
- Need for stronger research looking at international variation in obesity, dietary patterns, and physical activity, as relate to cancer risks and trends

Cancer survivors

- Better description of the natural history of diagnosed cancer in relation to body composition and physical activity
- Better understanding of the specific needs of cancer patients and survivors in terms of physical activity and weight loss studies

Translation into practice

- Need to understand how to use biomarkers in clinical settings
- Future research emphasis should not only be about discovery but also about clinical utility and strategy implementation
- Need to integrate basic science into clinical and epidemiological studies – and vice versa

Conclusions

Overall the conference proved successful and effective, with participants excited at the prospect of their research activities being integrally informed by the activities of others from different disciplines.

There was consensus to work together to build the infrastructure to support these transdisciplinary research activities in this area and we will consider how best to progress this.

“[The Conference was] a stepping stone for more transdisciplinary work in mechanistic and epidemiological research”

Concluding remark from the scientific committee (reflecting delegates comments)