

Appendix 4

Workshop Results

Breakout Session 1a

What are the top 5 critical societal issues relating to obesity, in terms of the well-being of the citizens of Europe?

Common points between the three breakout groups.

1. HEALTH, HEALTH SERVICES AND HEALTH CARE CONSEQUENCES

HEALTH

-Obesity is a core primary problem of other diseases and must be recognised as an independent medical condition e.g. heart disease, bone disease etc.

HEALTH SERVICES

Primary Prevention

-Children/adolescents/adults - with special focus on children and adolescents

Secondary Prevention

-Targeting high risk subgroups in the obesity population

-Services are failing (need new multi-disciplinary approaches)

Evaluation

-Data and standards must be put in place to evaluate successful strategies

HEALTH CARE CONSEQUENCES

-Many of the consequences of obesity are not addressed, e.g. physical and psychological, quality of life – stigma, social discrimination and loss of human resources

2. THE ECONOMY

DIRECT AND INDIRECT COSTS OF OBESITY AND THE ECONOMICAL CONSEQUENCES

-Increased health-care costs of co-morbidities

-Lower work productivity

-Loss of human resources

-Loss of competitiveness

OPPORTUNITIES FOR INDUSTRY (PHARMACEUTICAL AND FOOD) TO DEVELOP

-Industrial competitiveness and regulation of (a) treaters and (b) causers

-Development of different treatments and health-care services

- Improved food quality and functionality
- Improved food marketing and surveillance especially for children
- Standardised food portion sizes - from home to the supermarket

3.SOCIAL ASPECTS OF OBESITY

SOCIETAL VALUES

- Polarisation of society - low class obese/higher class
- Conflict industry or production versus needs of people
- Is obesity a moral or health problem?

ENVIRONMENT (OBESIGENIC) AND SOCIAL ENGINEERING

- Physical activity
- Urban planning especially with respect to exercise

PSYCHOSOCIAL ISSUES

- Health and well being

CONSUMERS

- Government policy
- Food perception (including orosensory and orofractory perceptions) and activity
- Societal impact
- Cultural context
- Self esteem
- Personal freedom vs social control

4.SCIENCE

- Research including spin-offs into other related fields and broad, wide ranging impact – behaviour/gene/metabolism/social
- Use a more integrative approach of disciplines (networks of excellence) and countries but considering the specificity's of countries and regions

5.EDUCATION AND COMMUNICATION

- Obesity is more prominent in less privileged social classes need to strategically target these areas
- Industry to inform on the content of products and consequences to health
- Excess and waste of food as an ecological burden
- Consistency of dietary advice
- There is a need for a good teaching paradigm

Why Europe?

Europe provides the natural experiment because of its diversity in culture and social issues aswell as

lifestyles, political and economical aspects.

Breakout Session 1b

In this light, provide a holistic vision of the Obesity European Research Area of the future.

Q1 - Ideally, what would European obesity research have accomplished in 10 years time?

1.EXPLANATION OF OBESITY EPIDEMIC THROUGH UNDERSTANDING

-Physiology (*in vivo* and *in vitro*)

-Molecular mechanisms of energy control including genes and gene development and the influence of genetic background and ethnic related issues

-Environmental triggers

-Psychology of obesity

-Gene-drug interactions

-Mechanisms of dietary approaches to weight management

-Interaction of genes on polygenic obesity, genes/environment

-Mechanisms of derived anomalies of plurimetabolic syndrome

-Perinatal programming in relation to obesity at biochemical, cellular and behavioural levels

-Different kinds of obesities

-The impact of nutrients in food on polygenic obesity particularly in early life

-Of individual susceptibility to obesity, its progression and co-morbidities

-Of the attitudes/beliefs of consumers

-Natural history of diseases of weight through functioning surveillance of physical activity, anthropometry and body composition

-Why some treatments for obesity are successful or unsuccessful.

2.PREVENTION

-Evidence based lifestyle and weight management intervention and evaluation

-Needs assessment – motivation/illness perception

-Dietary behaviour integrated and evaluated in education

-Appropriate/effective public health nutrition strategies for primary prevention, including the role of genetic variability in identifying individualised diet/drug therapy

-More effective social marketing and communication strategies

-Improve knowledge on eating frequency, diet composition etc for obesity prevention

-Innovative products/fitness tools

3.TREATMENT

-Effective treatments tailored for susceptible groups

-Formulation

-Diagnostic tools (cause/treatment)

-Predictive abilities

-Systems to measure impact of treatment strategies

-Develop new markers of obesity and new targets for drugs

-Develop realistic strategies to stabilise or prevent obesity

4.SCIENCE

-System to prioritise research

-Identification of a number of molecular targets through to clinical trials

-Databank

-Defined outcomes and processes to measure effectiveness of interventions

-Identification of biomarkers for obesity-related complications

-Scientific basis to communicate and educate = strategies to transform research to action

-Use of common methodology for epidemiological surveys.

Q2 - What challenges should European obesity research be able to tackle in 10 years time?

1.REVERSE THE TREND IN OBESITY PREVALENCE

-Halt (adults and children) and reverse the trend in childhood obesity

-Early intervention before obesity development

-Provide guidelines for developing countries to contain their obesity problem

-Identify clear environmental triggers

-Impact of rapid change in lifestyle on prevalence of obesity

-Identification and quantification of different risk factors

2. SERVICES

-Better health care delivery with increased social and educational projects

-Acceptance and greater awareness of obesity as a disease by all health care professionals

-Better education of mother and young

-Prevention through social and educational policy

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3. PREVENTION AND TREATMENT STRATEGIES

- More tailoring to the needs of the individual or defined sub-groups of the population
- A greater choice of drugs on the market
- Integrate emerging knowledge in genomics into primary prevention and treatment of obesity.
- Identifying optimal/appropriate dietary and physical activity strategies for specific susceptible profiles or subgroups
- Provide strong evidence-based guidelines for prevention and treatment of obesity to policy makers – provide options for the difficult choices to be made.
- Personalise strategies for treatment, due to polygenic nature of obesity.
- Select subgroups for action.

4. SCIENCE

- Design and execute a longitudinal EU wide study on the natural history of obesity
- Illustrate acceptability and utility of genotyping knowledge (e.g. risk co-morbidity)
- Prepare the next generation of scientists to stabilise research and promote training
- Integration of disciplines and transfer knowledge of obesity to other fields.
- Promotion of European success to become worldwide model.

Q3 - What should the shape and nature of the European obesity research community be?

1. Europe wide networks for obesity research – investigate optimal size for maximal reactivity
2. Centre for Excellence (single or multi-site) in obesity research and training (formation of professional clinical researchers)
3. Funding and technology resources
 - Integrate national and EU research funding to create a co-ordinated network of integrated research, which is multi-disciplinary and has critical mass.
 - Discover optimal size for European collaborative projects
 - Rapid response funding to be made available (smaller projects)
 - Infrastructure in genomics funded and developed
4. Standardised experimental methods for research including clinical trials (large scale studies on prevention including non pharmacological approaches) and good research practise to ensure total objectivity and transparency.
5. It should integrate human and animal studies and also studies at molecular and whole body level – inter-disciplinary training should be introduced.
6. Extensive access to biological resource bank (including tissue material and biological resources).
7. Multi-dimensional researchers with clinical/research background including

behavioural, social and economic scientists

8. Implement targeted problem solving approaches versus traditional approaches

9. Flexible feedback system for information (e.g. multilingual)

10. Improved communications - especially between

-policy makers in EU and academia, industry and member states

-medical researchers and clinicians

-experimental medicine and drug discovery process

Q4 - Why is this vision important to Europe? What impacts on society will be felt, or in progress, in 10 years time?

1. We should have had an impact in alleviating the economic (decrease in health-care costs and increase in new products), social and physiological burden of obesity and related health problems and have begun to address related inequalities in health within and between countries

2. Increase quality of life

-Reduce burden on the poor

-Increase productivity

-Reduce the stigma of the disease

3. Understanding of obesity integrated into broad areas of public policy

4. We should see an impact on many elements of the food chain from primary production to processing

5. Identification of actionable and necessary environmental and ecological changes

6. There should be more input to policies for widening societal trends

7. To have people better educated in nutrition and in the ways in which obesity develops

8. To identify cohorts in which obesity should be a benefit (biological diversity).

Q5 - To achieve this vision for the status of European research in 10 years time, what 3 key research challenges need to be addressed now?

GROUP 1 – GENOMICS AND BIOTECH

1. Knowledge of Causes and Processes

-Convert the mass of information into knowledge

- Increase understanding of
- Genes and gene networks
- Brain mechanisms -including reward, preferences, motivation, adherence
- Co-morbidity – risks – dangers
- Interactions: Gene/Nutrient/Development/Environment
- Importance of dietary components and composition tailored for age, ethnicity etc.
- Normal energy homeostasis
- Relationships between obesity complications (why is it so dangerous to be obese)
- Adipose tissue development, metabolism and endocrine role
- Identification of predictive biomarkers for co-morbidities
- Sensory perception of food and appetite regulation

Which of the above are modifiable?

- Target biological and social process that can be changed.

2. Natural Experiments

- How to have an impact on changing individual lifestyles
- Lean/obesity resistant individuals
- Side effects of neuroleptics
- Obesity and diabetes and smoking cessation
- Improve cross talk with other diseases
- Increased number of long-term (3-5 year) clinical and prevention studies with special reference to cost and participant compliance
- Address the question of 'Why are dietary intervention trials so difficult'

3. Technology

- Data proliferation – knowledge and statistical methods (development of data mining).
- Establish well managed tissue banks – standardised phenotyping (ethical issues)
- Global standards for experimental methods.
- Develop animal models.
- Large scale work – numbers and time.
- Validation of druggable gene targets and metabolics.
- Identify biological processes to use as 'tools' of genomics and biotech methods, NEW DRUGS, FUNCTIONAL FOODS

GROUP 2 – IMPROVING DIET THROUGH HEALTH AND PHYSICAL ACTIVITY

1. Establish a European Obesity Research Institute.

2. Plan a multi-centred randomised control trial incorporating all elements of weight gain/loss/regain/oscillation – involving diet/physical activity, genomics, etc.

3. Have clear objectives for the evaluation and validation of different types of intervention/treatment strategies.

GROUP 3 – EARLY NUTRITION AND PROGRAMMING

1. Perinatal programming

- molecular basis, mechanisms

- time windows

- perspectives of prevention

- in animal models and human groups

2. Focus on childhood obesity epidemic

3. Exploitation of the large epidemiological cohorts available in Europe

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Breakout Session 2

What research needs to be done in the next 5-10 years to address challenges and achieve this vision? What "building blocks" of research are needed?

GROUP 1

Q1 - What are the key research areas to be addressed?

1. Identify genes for a genetic network (including gene expression and proteomics)

2. Co-morbidities

- Links with obesity

- Identification of biomarkers

3. Interactions

- Gene

- Environment (including nutrition)

- Physiology (including brain, adipose tissue and energy metabolism)

GROUP 2

1. Multi-centre multidisciplinary randomised control trial

2. European obesity research institute
3. Public health nutrition strategies for intervention in obesity
4. Restrained eating/foetal programming
5. Mis-reporting of food intake
6. Physiology of catch-up growth

Selected 1 and 2 for further discussion – does not imply any judgement of priority.

Multi-centre RCT, multidisciplinary

For a large multi-centre RCT on diet, lifestyle, behavioural & genomic influences on weight change, the following would need to be considered (for example)

- The intervention e.g. fat levels, glycemic index issues, physical activity, behavioural issues etc.
- The study population e.g. age, family history, co-morbidities
- The method e.g. would centralised supervision of food choice be possible – like the CARMEN study
- Which genes would be examined in screening
- Which metabolic end points would be selected
- What are the key determinants of weight control?
- What will be the clinical significance of the intervention?
- What is the minimal physical activity to maintain healthy weight?
- What strategies will be used to gain compliance on the intervention?
- Will there be a genetic and lifestyle component to the intervention?
- What is the impact of dietary responses on molecular physiology

GROUP3

1. Perinatal programming (score – 13)

2. Childhood obesity (score – 12)

3. European epidemiology study (score – 7)

4. Categorise types of obesity (score – 6)

5. Sensory perception (orofactory etc.) (score – 5)

6. New drugs and food (score – 3)

7. Integration (score – 0)

Selected top 3 further discussion see below

Q2 – What key research questions need to be addressed?

GROUP 1

1. Genes and Genetic Networks - How does obesity happen and how to prevent it – what is the genetic mechanism?

- Identify major gene effects (10 years)
- What are all the genes involved in (i) energy balance; (ii) food choice; (iii) activity (10 years +)
- Generate normal references for all ethnic groups (5 years)
- Identification Capabilities
 - Human and animal genetic screening – QTL
 - Animal models – random mutagenesis/transgenic
 - Linkage/fine map/association/sequence
 - Genome wide association (SNP/LD map)
 - Functional genomics – profiling mRNA/proteins
- Validation
 - Extend existing techniques
 - Profile mRNA and protein

2. Co-morbidities

- Effect of co-morbidity treatment on obesity (10 years)
- Is there an overlap between obesity and comorbidities and genetic networks? (10 years)
- Why are different compartments of adipose tissue important? (10 years)
- Impact of decreasing obesity on complications
- Data on other methods of weight loss (e.g. surgery) - is weight loss healthy? (+10 years)
- Are complications fully reversible? (+ 10 years)
- Can we find genes that predispose to complications? (better than family history? (5 years)
- Can we find blood borne markers that detect and/or predict complications? (+10 years)

3. Interactions: Gene/Environment/Physiology

- Merge animal and human work. Benefits and logistics of this merger. (5 years)
- Use experimentally-sensitive designs to look at gene/ environment/ development interactions. These must be able to cope with complexity and variability of the interaction. (5 years).
 - For example – Diet induced obesity
- What are the mechanisms for the epigenetic effects? (10 years)
 - For example – are the effects seen in mice the same for humans?
- Establish functional tests as a measure of human phenotype (5 years)

GROUP 2

- What are the key determinants of weight control?
- What will be the clinical significance of the intervention?
- What is the minimal physical activity to maintain healthy weight?
- What strategies will be used to gain compliance on the intervention?
- Will there be a genetic and lifestyle component to the intervention?
- What is the impact of dietary responses on molecular physiology

GROUP 3

Perinatal programming

Years	Research Question	Linkage
5-10	Prove/disprove perinatal link to obesity	D
5-10	What are the causal factors at the level of adipose tissue, precursor linkage identification & programming?	D
5	What are the other causal factors of obesity (smoking)?	G
5-10	What are the critical time windows?	G,D
5-10	What are the mechanisms of programming?	G,D
5	What is ethically possible in human (animal)?	

G – genomics (group 1); D – diet (group 2)

Childhood Obesity

Years	Research Question	Linkage
5-10	What is the impact of environment vs genetics?	G,D
<5	What impact will improvement in education pathways have on development of obesity?	D
<5	What impact do food products & dietary habits have on obesity?	D
<5	What is the role of diversification of foods (e.g. weaning)?	D
5-10	How do children acquire sensory experiences?	G
5-10	What are factors that can produce a rebound in childhood obesity?	G,D
5-10	What is the mechanism responsible for regulation of childhood obesity?	G,D
<5	What is the role of diet and physical activity in early life?	G,D
5-10	What is the time-scale of expression of obesity-related complications (early markers)?	G,D

G – genomics (group 1); D – diet (group 2)

European epidemiology

Years	Research Question	Linkage
<5	Can the development of obesity be characterised through different exposures?	D
<5	Can we identify the determinants of exposure in different countries, populations?	D
<5	Is there a threshold of overweight at which stability persists, and if so why?	G,D
<5	What is the yearly increase in BMI in different countries?	G,D
<5	How often can we measure BMI? (or other indices)	D
5-10	Explore the potential of prevention and therapeutics in different countries	D
<5	How can we improve and enlarge the existing cohorts of follow-ups?	D

G – genomics (group 1); D – diet (group 2)

Q3 - What technologies need to be developed

1. Genomics and proteomics

- High throughput functional genomic techniques
- Combinations of gene expression and imaging studies
- Develop reference profiling for functional genomics
- Tools for animal model phenotyping
- Integrated platform for validation – functional genomics

2. Mathematical modelling – neural network of metabolism

3. Miniaturisation e.g. for biopsies
4. Animal models to study inter-organ interactions
5. Bioinformatics
6. Delivery – tissue/organelle
7. Effective markers of compliance to the intervention strategy
8. Energy balance as an intervention outcome – are there biomarkers?
9. How do we conduct very long term intervention trials (>4 years) and can we use traditional tools?
10. Can we use resource-efficient data collection e.g. barcodes, internet, palm pilots etc.?
11. Better laboratory reference techniques and field techniques for body composition, energy balance and food reward systems.
12. Can we sample blood automatically in ambulatory circumstances to avoid dependence on fasting blood samples?
13. Repeated longitudinal measure of gene expression in muscle/adipose tissue.
14. Strategically linking animal and human models efficiently.
15. Non-invasive technologies to look at fat mass, body composition, foetal growth of organs
16. Metabolic tools, with stable isotopes
 - Transfer of nutrients across placenta
 - Metabolic differences in children

Q4 - What new research directions need to be explored

1. Integration of functional genomics with epidemiological and large-scale clinical trials.
2. Real-time measurement of metabolism in vivo
3. Influence of nutrients on epigenetic effects
4. Learn from redundant pathways and explore non-redundant pathways
5. Lifecycle of fat cells: fate of stem cell development
6. Use of different animal models e.g. gene trapping by random mutagenesis
7. How to speed up animal functional tests to validate genes
8. Methods to assess subjects "well being"
9. Metabolics – over long time scale/functions

10. Molecular understanding of food preference
11. Statistical and mathematical modelling of many areas in the diet/lifestyle/obesity link
12. Role of other dietary ingredients
13. Examine liver function through imaging techniques
14. High throughput screening of food ingredients for e.g. insulin effects
15. Stereo-specific effects of newly synthesised isomers of nutrients – e.g. the new ‘CLAs’
16. Cognitive behavioural therapy for long-term effects
17. Examine the role of nutrient partitioning in food consumption habits
18. Sexual activity and food habits
19. How to treat foetal malnutrition syndrome?
20. Childhood obesity: Examine the change in food composition retrospectively using epidemiological studies e.g. quality of fatty acids and dietary calcium
21. New animal models in addition to rat and mouse
22. Obesity in pet animals and relation to childhood obesity

Q5- What existing areas of research need to be expanded?

- Food consumption under-reporting
- Periodicity of eating (intradian, ultradian)

Q6 - What linkages need to be made?

1. Novel, easy, cheap ways of phenotyping subjects
2. Tools to assess how the body is composed at different points in time (engineering).
3. Use other epidemiological samples for data e.g. those collected in CHD & cancer studies
4. Understand linkage between nutrition and genomics
5. Understand the interaction of obesity and (i) psychiatric and eating disorders (ii) sociology and (iii) exercise physiology
- 5 Common biobank
6. Info on diet changes e.g. maternal diet
7. Biomarkers

Research specialities

