



**Interdisciplinary Public Health Seminar
EHESP Public Health Doctoral Network**

**Diabetes and obesity:
Current understanding and perspectives for
2030**

**Assessment and discussion of strategies for the two
related public health challenges of the 21st century**

**Friday, January 23rd 2015
10:00 AM – 5:30 PM**

Registration desk from 9:30 AM

ISPED, Université de Bordeaux, 146 rue Léo Saignat
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- ISPED : Carole Dufouil, Pascale Barberger-Gateau, Pr Genevieve Chêne
- Structure Fédérative de Recherche (SFR) Santé Publique, Société : Pr Roger Salamon



PROGRAM OVERVIEW

9.30 – 10.00 COFFEE & REGISTRATION

10.00 – 12.00 SESSION 1: WHAT IS THE PROBLEM?

CHAIR : **PASCAL BARBERGER-GATEAU**, INSERM U897, BORDEAUX, FRANCE

10.00 – 10.10 Welcome & Opening session

Judith Mueller, EHESP, Rennes, France

Geneviève Chêne, AVIESAN, INSERM U897, Bordeaux University, France

10.10 – 10.30 Epidemiological context: Diabetes and Obesity

PhD Students of the Organizing Committee

10.30 – 11.00 Geographical environment, work economic sector and obesity

Antoine Lewin, INSERM U1136, Paris, France

11.00 – 11.30 Selected genetic aspects of type 1 diabetes incidence and clinical course of disease among children Europe vs. Pomeranian region of Poland

Malgorzata Pawlowicz, Medical University of Gdansk, Poland

11.30 – 12.00 Diabetes: Applying multistate models with multiple timescales

Bendix Carstensen, Steno Diabetes Center, Gentofte, Denmark

12.00 – 13.15 LUNCH BREAK

13.15 – 15.15 SESSION 2: WHAT ARE THE RISK FACTORS & CONSEQUENCES FOR DIFFERENT AGE GROUPS?

CHAIR: **CAROLE DUFOUIL**, INSERM U897, BORDEAUX, FRANCE

13.15 – 13.45 Vitamin D during prenatal life and risk of later development of type 2 diabetes

Amélie Cléo Keller, Institute of Preventive Medicine, Copenhagen, Denmark

13.45 – 14.15 Roles of diet quality and physical activity in preventing functional decline in diabetic older adults

Berna Rahi, INSERM U897, Bordeaux, France

14.15 – 14.45 Individual and collective strategies to cope with diabetes: perspectives from the African continent

Annick Tijou-Traoré, LAM Les Afriques dans le Monde UMR5115, Bordeaux, France

14.45 – 15.15 Diabetes in adults

Vincent Rigalleau, INSERM U897, Hospital Haut Lévêque, Bordeaux, France

15.15 – 15.30 COFFEE BREAK

15.30 – 17.30 SESSION 3: INTERDISCIPLINARY APPROACHES AND PERSPECTIVES

CHAIR: **GENEVIEVE CHENE**, AVIESAN, INSERM U897, BORDEAUX UNIVERSITY, FRANCE

15.30 – 16.00 Children obesity prevention and treatment from clinical and public health perspectives

Michal Brzezinski, Medical University of Gdansk, Poland

16.00 – 16.30 Lessons learned from specialized obesity centers in France

Erell Pencreac'h, General Directorate for Healthcare Provision, Ministry of Health, France

16.30 – 17.00 The way forward: Interdisciplinary and European research collaboration efforts in the field of obesity

Jean-Michel Oppert, Department of Nutrition, Pitié - Salpêtrière University Hospital, Paris, France

17.00 – 17.30 Round table

17.30 – 17.45 CONCLUSION AND CLOSING REMARKS

DETAILED PROGRAM

SESSION 1: WHAT IS THE PROBLEM?

CHAIR : Pascale Barberger-Gateau

Inserm U897, Bordeaux France

Geographical environment, work economic sector and obesity

Antoine Lewin

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Given the limits of the international literature on the environmental disparities in obesity prevalence (focused on the residence neighborhood) and considering the lack of empirical studies in France, we have been interested in the relationships between, first the residential and professional neighborhood characteristics and the work economic sector, and secondly between two body fat indicators: the Fat Mass Index (FMI) and the percentage of Fat Mass (%FM). Then we compared the effects of the work economic sectors on several cardiovascular risk factors. Finally using a longitudinal study, we evaluated the links between socioeconomic variables and the evolution of the anthropometric parameters among participants of the RECORD Study. Simultaneously, our methodological objective was to explore the attrition biases due to missing data in longitudinal studies.

In the first part of this work, data of 4331 people from the RECORD Study, localized at their residence and at their workplace, were analyzed. Body composition was assessed using a bioelectrical impedance analyzer. Multilevel regression analyses were used to study the determinants of FMI and %FM. Results showed that, after adjustment, for men, the FMI and the %FM increased while the residential neighborhood population density and education level decreased. For women, the education level was negatively associated with the %FM. For men, weaker FMI and %FM were observed on people working in construction or in the communication/transports sectors compared to those working in the education sector. For women, the FMI was higher for those working in the public or in the health and social sectors rather than those working in the transport and communication sector. A long home-work distance was associated with a high FMI for women. Moreover we showed that the BMI was not able to fully capture the effects of the work economic sectors on the fat mass.

In a second part, data of 4360 employed people from the RECORD survey have been analyzed. Ten cardiovascular risk factors were assessed: body mass index (BMI), waist circumference, systolic and diastolic blood pressure (BP), pulse pressure, total cholesterol, glycaemia, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and resting heart rate. Multilevel linear regression models stratified by sex and adjusted for individual and neighborhood sociodemographic characteristics were estimated.

Among men, the Health and social work sector was found to be the most protective sector for BMI, waist circumference, and glycaemia (while the Construction sector and the Transport and communications sector tended to be unfavorable for these outcomes). The Health and social work sector was also associated with a higher HDL cholesterol among men. However, men working in the Health and social work sector showed the highest systolic BP and pulse pressure. Women working in the Health and social work sector had the highest BMI, the largest waist circumference, and the most elevated systolic and diastolic BP. The Commercial and repair of vehicles sector, the Transport and communication sector, and the Collective, social, and personal services sector were associated with a more favorable profile for these risk factors among women. In conclusion, there were no work economic sectors associated with increase risks for both women and men for all or most of the examined risk factors.

Selected genetic aspects of type 1 diabetes incidence and clinical course of disease among children - Europe vs. Pomeranian region of Poland

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Type 1 diabetes (T1DM) is a strictly organ-specific autoimmune disease, where selective destruction of only pancreatic β -cells producing insulin is developed. This process occurs progressively in genetically susceptible individuals after a precipitating event (usually environmental trigger). The first clinical symptoms of diabetes appear, when nearly 80-90% of the β -cells have been destroyed. The prevention methods to preserve endogenous insulin production are still under investigation. The results of epidemiologic and genotype-phenotype studies could help to perform some T1DM prevention strategies.

Globally the T1DM incidence is the highest in Europe, with the specific northwest – southeast gradient (EURODIAB study 1989-2008). This gradient conversely corresponds with the conformation of decreasing heterozygosity isoline in European subpopulations (Lao *et al.* 2008), which is especially apparent in the comparison of north and south regions of Poland.

T1DM is a polygenic disease determined mainly by HLA linked genes, but also by several non-HLA loci. From non-HLA loci the *PTPN22* gene and its polymorphic variants (e.g. c.1858T>C – rs2476601) play a crucial role. The enzyme isoform coded by the *PTPN22* c.1858T allele is considered as a gain-of-function phosphatase form, causing setting thresholds for signaling through the TCR/BCR receptors and therefore disturbances in all lymphocytes subpopulations. The distribution of the *PTPN22* c.1858T allele with a north-south gradient could explain some changes in T1DM incidence in Europe over the last decades.

In comparison with European countries the Pomeranian population appears to be especially genetically predisposed to T1DM development due to significantly different distributions of some genes polymorphisms associated with T1DM pathogenesis. The *PTPN22* c.1858T>C polymorphism with unusually high frequency of T allele (21.17%) and its sex-specific manner effects to the clinical course of T1DM could be a good example. The specific polymorphic variants distributions in Pomeranian region could be explained by the founder effect caused by ethnographical and historical factors.

Diabetes: Applying multistate models with multiple timescales

Bendix Carstensen

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The Danish National Diabetes Register covers the period from 1995. Linking with the mortality register makes it possible to assess the mortality among diabetes patients as a function of age, calendar time and duration of diabetes. Linking with the national mortality statistics for the entire population further allows us to assess the standardized mortality ratio, i.e. the relationship between mortality among persons with and without diabetes.

It turns out that mortality among diabetes patient is substantially elevated during the first year after diagnosis of diabetes, and subsequently stabilizes at a level above the population mortality that is constant, but dependent on the age at diagnosis. The younger the age at diagnosis, the higher the mortality ratio to the general population; 1.9 for persons diagnosed at age 50, 1.4 for persons diagnosed at age 65 and no excess risk for persons diagnosed at 80 and over.

Linkage with the Danish Cancer Registry enables us to assess how duration of diabetes and duration of insulin usage influences the cancer incidence rate-ratio between persons with and without diabetes. Further linkage with mortality data allows calculation of the cumulative risk of cancer from a given age.

It turns out that also the cancer incidence rate-ratio is higher in the initial period after diagnosis of cancer and also in the period after initiation of insulin therapy, and stabilizes at a level 15-20% above that of the non-diabetic population. But due to the elevated mortality among diabetes patients, the cumulative risk of cancer is the same for persons with and without diabetes.

Finally, the access to combined diabetes and cancer data allows calculation of life-time risk of both diabetes and cancer – a calculation parallel to the classical demographic concept of expected life time.

The lifetime risk of cancer is currently (2012) close to 50% and of diabetes some 40%, while the lifetime risk of both slightly less than 20%. These figures have increased substantially since 1995 where the lifetime risk of cancer and diabetes were 35 and 20% respectively, and of both diseases around 6%. This reflects both the increasing incidence rates of diabetes (4% per year) and cancer (2% per year) and the decreasing mortality (4% per year).

SESSION 2: WHAT ARE THE RISK FACTORS & CONSEQUENCES FOR DIFFERENT AGE GROUPS?

CHAIR : Carole Dufoir
Inserm U897, Bordeaux France

Vitamin D during prenatal life and risk of later development of type 2 diabetes

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Vitamin D deficiency is common among otherwise healthy pregnant women and may have consequences for them as well as the early development and long-term health of their children. However, the importance of maternal vitamin D status on offspring health later in life has not been widely studied. The present project includes an in-depth examination of the influence of exposure to vitamin D early in life for development of child and adult diseases such as fractures of the wrist, arm and clavicle; obesity; schizophrenia; type 1 and type 2 diabetes during child- and adulthood.

The study is based on the fact that in 1961 fortifying margarine with vitamin D became mandatory in Denmark. Apart from determining the influences of exposure prior to conception and during prenatal life, we will examine the importance of vitamin D exposure during specific seasons and trimesters, by comparing disease incidence among individuals born before and after fortification. The Danish National databases assure that there are a sufficient number of individuals to verify any vitamin D effects during different gestation phases. Additionally, a validated method will be used to determine neonatal vitamin D status using stored dried blood spots (DBS) from individuals who developed the aforementioned disease entities as adults and their time and gender-matched controls.

The results of the study will contribute to our current understanding of the significance of supplementation with vitamin D. More specifically, they will enable new research in related fields, including interventional research designed to assess supplementation needs for different subgroups of pregnant women. Also, other health outcomes can subsequently be studied to generate multiple health research opportunities involving vitamin D. Finally, the results of the study will justify the debate of Danish health authorities whether to resume vitamin D supplementation policies.

Adapted from: Jacobsen et al. (2013) The influence of early exposure to vitamin D for development of diseases later in life. BMC Public Health 2013, 13:515 doi:10.1186/1471-2458-13-515

Roles of diet quality and physical activity in preventing functional decline in diabetic older adults

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Aging increases the risk of muscle strength (MS) loss, type II diabetes (T2D), and functional capacity (FC) decline. Independent of aging, diabetic older adults (OA) are at increased risk of MS loss and FC decline compared to their non-diabetic counterparts. Nutrition is a determinant of optimal aging and is important in managing diabetes. It also minimizes MS losses and modulates FC decline. In addition, physical activity (PA) offers benefits similar to those conferred by nutrition. Therefore, our main objective is to present the roles of diet quality (DQ) and PA in FC maintenance in community-dwelling diabetic OA in secondary analyses of the NuAge cohort.

Among 243 diabetic OA, DQ alone was not associated with MS or FC declines over the three year follow-up. However, DQ combined with PA showed associations with upper body MS. Specifically, good DQ combined with maintenance of PA over follow-up was associated with minimal MS losses in diabetic older men compared to others. However, no significant results were found for lower body MS in either males or females. Furthermore, DQ combined with PA was not associated with FC in these participants. Finally, our results have shown that adequate energy and protein intakes are associated with FC maintenance. In fact, diabetic older men with energy intakes of 30 kcal or greater/kg body weight experienced lesser declines in FC compared to those having inadequate energy intakes, however, significant effects were lost after adjustment for weight change. Diabetic older women with protein intakes of 1g or more/kg body weight had minimal declines in FC compared to those with inadequate protein intakes. Finally, we have shown that adequate protein intakes minimized lower body MS losses in diabetic women in the NuAge cohort.

Taken together, these results provide evidence that good DQ, adequate energy and protein intakes and the practice of PA are all factors that can minimize MS losses related to aging and accelerated by T2D, and hence maintain FC in diabetic OA. Nevertheless, further research is needed to confirm these results.

Experience, expectations and strategies of diabetic patients in Bamako (Mali) How does policy shape diabetes (self-)management and leads to suffering

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Chronic diseases are steadily increasing in the world. This is also true for Africa, but with a particularity that health systems are historically more organized for the management of acute illnesses. Thus, chronic pathologies with their implications on a long-term follow-up and support, increase difficulties not only for the health care systems but also for the patients in their everyday life.

Based on data from a Sub-Saharan African country, Mali, and for a given pathology, diabetes, my purpose in this presentation is to interrogate the incidence of the difficulties of the health system and public health strategies that, by experience, are followed by expectations and individual and collective strategies of patients with diabetes type 2 treated in a biomedical health structure in Bamako.

I focus here on data from two anthropological research studies realized in Bamako¹. These data are the results of the study I conducted among patients during these research projects. Putting in perspective diabetes with HIV provides an opportunity to distinguish the burden of the nature of the pathology in the management of a chronic health problem.

The perception that patients have of their disease is an illustration of interactions between policy and their own management. Under the weight of a disease which seems for them too belatedly recognized by international and national authorities, the patients qualify their disease as one of the worst that can exist. Hence the chronic nature of the diabetes can be particularly intimidating, contrary to HIV.

The study of patients' disease experience and the accompanying routine care show how organizations of diabetes care and social impacts are involved in the emergence of moral suffering and fears related to the disease and care. These feelings retain even more attention from patients who consider sedation as an essential element in the care of diabetes. However, the protocols of the national health policies and those set up by the management structure do not offer any resources to help patients to soothe their suffering. Yet, it is often in the care structure that patients seek an answer to this need of relief, especially from the doctor and other patients.

To manage their condition in accordance with the constraints and needs imposed by their chronic disease, most of the diabetic patients seen during this study consider that being followed by the same doctor is an essential aspect of their care. Relations between patients play also a vital role in the construction of the relationship with the care and the disease. Finally, they also develop individual strategies to achieve it. Some of these strategies have induced social consequences. These expectations, these strategies show how far these patients are from remaining passive and suffering from the political constraints.

¹ Equipe programme de recherche 1 (ANR) : I. Gobatto, A. Tijou Traoré, R. Besson, Bernard, B., J. Martini, A. Fligg, B., Toumanion. Equipe programme de recherche 2 (Sidaction) : I. Gobatto, A. Tijou Traoré, J. Martini

Diabetes in adults

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Due to changes in our lifestyle, we are gaining weight, and as our life expectancy rises, the prevalence of diabetes increases: since the 1970's, for a middle-aged person, the risk of becoming diabetic has almost doubled. There are two main types of diabetes: Type 2 accounts for more than 90% of cases, followed by Type 1, usually they are well distinguished based on simple clinical criteria. Their common definition is "chronic hyperglycaemia (>1.26 g/L) with a risk of vascular complications". The control of glucose and co-factors (arterial pressure, blood lipids...) reduces by ~50% the risk of these complications.

However some patients already have complications at diabetes onset, and some progress despite good glucose control. The main explanation for these bad cases is "metabolic memory": during previous years of inapparent hyperglycaemia, Advanced Glycation End-products (AGEs) accumulate in tissues, where they still exert deleterious effects despite the patient is well-treated.

Since 2004, the evaluation of this metabolic memory has become possible for the clinician and for the epidemiologist. As most AGEs are fluorescent, their concentration in tissues can be assessed from the quick, simple, low-cost and non invasive measurement of the skin autofluorescence. Our presentation will show some examples of what we are learning from these measurements in patients with diabetes, in elderly subjects from the 3C cohort, and in pregnant women.

SESSION 3: INTERDISCIPLINARY APPROACHES AND PERSPECTIVES

CHAIR : Geneviève Chêne

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Children obesity prevention and treatment from clinical and public health perspectives

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Overweight and obesity can be seen from many perspectives. The most often ones are: individual-clinical, public health, economic, social. These views differ in many aspects.

In case of children obesity the problem has a bigger context as we have many less possibilities of intervention and a much more complex, developing organism.

Very often the common perception of obese child is that is a lazy, physically inactive, and eating only junk food. That she/he (and parents) is responsible for what is happening to the health condition of this child. Not many clinicians or “publicity” sees this problem in a wider scenario. This child lives in XXI century – with all its benefits – easy access to food, decreased need for physical activity as all can be done thanks to widespread technology. In this complex environment it is very easy to gain weight if you forget (or not know) simple rules – that the energy that we eat needs to be used.

In the clinical perspective we need to remember about the socioeconomic context of obese child – he is more susceptible for social, economic and most important for health consequences. The most important is possibility of developing the metabolic syndrome with all scale of health issues but also higher risk of depression, low self-esteem. To work with this problems we need to involve the child (youth) but also his closest family and environment that he lives in.

That gives us the wider perspective of the socioeconomic context of obesity. To develop proper habits in the aspect of nutrition and physical activity and thru this do decrease the risk of obesity and its complications we need to change the local, regional, national and global level. The public health ladder of population interventions allows us to choose one or some of the steps for public interventions. From doing nothing to monitoring and education to law regulations. Some of them are evidence based and can be implemented directly to different environments. Which of them to choose? It is a simple question, but the answer differs depending on economic, political, financial conditions.

Lessons learned from specialized obesity centers in France

The French Obesity Plan (2010-2013) and Healthcare provision

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The French Obesity Plan (2010-2013) enabled the implementation of both an original and sustainable structure of healthcare provision and guidance for the management of obese subjects, including severe cases. Obesity affects between 1% and 4% of the French population.

Under the auspices of the regional health agencies (ARS), the organization of healthcare pathways by means of 37 specialized centers of obesity (CSO) has two objectives.

The first objective is to improve healthcare provision for people with severe obesity, by means of expert multidisciplinary teams, identified within health facilities that use adaptive equipment.

The second objective focusses on the creation of a network of stakeholders in the field of prevention and management of obesity as well as the organization of care networks, local coordination, and the adaptation of equipment (including bariatric transportation). In this perspective, among key issues are the accessibility, intelligibility and gradation of care. The latter entails that care is delivered at the right place, involving the general and/or liberal healthcare practitioner, healthcare facilities, providing medical, surgical or post-operative and re-education care to the obese patient.

By means of healthcare provision structures that have gained visibility and cooperation efforts, the Obesity Plan has allowed the unprecedented mobilization of healthcare professionals and the creation of new synergies. The latter are conditions for the implementation of a new approach to obesity medicine and surgery based on novel cooperative practices.

The way forward: Interdisciplinary and European research collaboration efforts in the field of obesity

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Obesity is recognized as a global epidemic. Despite significant recent research investment, obesity prevalence rates continue to rise throughout most countries of the world, not least in Europe. The disease represents a heavy burden not only on individual citizens themselves but also on health care systems, the efficiency of the workforce and society at large. Obesity research represents a large scientific field – from basic molecular science to public health and humanities – where researchers across Europe have been very active over the years and have gained world-wide recognition. The presentation will build upon the conclusions of a conference that took place a year and a half ago under the auspices of the European Association for the Study of Obesity (EASO, www.obesity.org)(Oppert et al. 2011). Key issues raised emphasized that 1) obesity is a gateway to the most prevalent non communicable diseases including but not limited to cardiovascular diseases, diabetes and some cancers; 2) obesity is a model for transdisciplinary research integrating social sciences and humanities to biomedical research; 3) in a time course perspective, obesity develops and impacts over the whole of the lifecourse; 4) along a strong social gradient, obesity affects the most vulnerable segments of the population; 5) in terms of innovation, obesity represents a large market for new products and economic growth in Europe. The scope of the obesity problem clearly calls for increased collaboration and coordination of research activities on obesity across Europe.

Oppert JM, Sørensen TIA, Hebebrand J, Woodward E, Blundell JE. Opportunities for European obesity research in the coming decade. *Obesity Facts* 2011; 4: 425-6.