EUBIROD TECHNOLOGY: RELATIONSHIP BETWEEN OBESITY AND DIABETES IN NEWLY DIAGNOSED TYPE 2 PATIENTS

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To benefit prevention, intervention and optimal overall patient care the aim of this study was to identify the risk factor of obesity in newly diagnosed Type 2 diabetes using the “European Best Information through Regional Outcomes for Diabetes (EUBIROD)” technology based on a novel software package tool for epidemiological studies and clinical trials. EUBIROD was a 21-country consortium EU DG-SANCO project developing a series of standardised diabetes indicators for reliable comparison across Europe, on which we acted as partner. The study sample was obtained from the National Institute of Diabetes “N. Paulescu”, Ambulatory Diabetes Centre, Bucharest. We used baseline data n=1797 newly diagnosed diabetes patients in 2010, n=903 (50.3%) male, and n=894 (49.7%) female. Results: In Type 2 diabetes, only 42 of 338 (12.4%), 127 of 900 (14.1%), 88 of 478 (18.4%) and 9 of 44 (20.5%) had normal BMI [18.5–25 kg/m²], 93 of 338 (27.5%), 271 of 900 (30.1%), 166 of 478 (34.7%) and 25 of 44 (56.8%) had elevated BMI [25–30 kg/m²], 199 of 338 (58.9%), 499 of 900 (55.4%), 220 of 478 (46.0%) and 10 of 44 (22.7%) had BMI ≥30 kg/m² respectively, for age band [25–50), [50–65), [65–80) and ≥80 yrs. A breakdown of the numbers of patients, Type 1 and Type 2, with BMI band and gender is as follows: 7 of 903 (0.8%) male and 8 of 894 (0.9%) female had BMI <18.5 kg/m², 161 of 903 (17.8%) male and 126 of 894 (14.1%) female had normal BMI [18.5–25 kg/m²], 328 of 903 (36.3%) male and 232 of 894 (26.0%) female had elevated BMI [25–30 kg/m²], 407 of 903 (45.1%) male and 528 of 894 (59.1%) female had BMI ≥30 kg/m². The technology is based on a European minimum common dataset and data dictionary has been developed that is applicable using existing clinical datasets for Diabetes. Results based on data evidence are an objective support for how future policy measures in these areas might be directed to benefit prevention, intervention and overall patient care. Efficiently and easy data analysis may facilitate our understanding of the pathophysiology of obesity and diabetes and what are targets and directions for further research.

Key words: diabesity, newly diagnosed diabetes, type 1 and type 2 diabetes, EUBIROD software, Open-source statistical language R, XML Schema, e-health applications, data integration.

INTRODUCTION

It is predicted that, by 2030, 366 million adults worldwide will have diabetes1. Given the magnitude of the problem and its consequences, this paper focuses on the link between diabetes and obesity, two of the most pressing health problems in the developed world. It covers topics ranging from the changing epidemiology of type 2 diabetes to an analysis of the principal causes of the metabolic syndrome. Obesity and low level of physical activity are emerging as an important public health problem that increases the risk of many health complications such as hypertension, hypercholesterolemia, coronary heart disease, and type 2 diabetes2,3. Type 2 diabetes mellitus (T2DM), associated with obesity, “Diabesity”, is today the most common form of diabetes. Diabesity is associated with a number of other cardiovascular risk factors which constitute the metabolic syndrome. Also, it is associated with a shorter expectation of life, increasing morbidities.
MATERIAL AND METHODS

Data Sources: In brief, individuals with type 1 and type 2 diabetes (WHO criteria) living in Bucharest, Romania, were selected from the Bucharest Ambulatory Register. The body mass index (BMI) were measured by weight (kilograms) and height (centimeters) and calculated by weight in kilogram divided by height squared (square meters). Individuals were categorized into underweight BMI < 18.5 kg/m\(^2\), normal-weight (BMI 18.5–25 kg/m\(^2\)), overweight (BMI 25–30 kg/m\(^2\)) and obese (BMI > 30 kg/m\(^2\)) groups. The anonymised records were collected on Excel spreadsheet, and a EUBIROD data set used for data exchange. We used baseline data n=1797 newly diagnosed diabetes patients in 2010, n=903 (50.3%) male, and n=894 (49.7%) female. As shown on Table 1 with the numbers of records and numbers of patients with an identified diabetes type and age band, created through EUBIROD package, mainly were recorded Type 2 newly diagnosed diabetes patients.
**Table 1**

<table>
<thead>
<tr>
<th>Type of diabetes</th>
<th>Age</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤15</td>
<td>(3.3)</td>
</tr>
<tr>
<td>Type 1</td>
<td>10 (2.8)</td>
<td>100 (5.2)</td>
</tr>
<tr>
<td>Type 2</td>
<td>2 (66.7)</td>
<td>2 (0.0)</td>
</tr>
<tr>
<td>Other Type</td>
<td>357 (19.9)</td>
<td>1797 (100.0)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>3 (0.2)</td>
<td>6 (0.3)</td>
</tr>
</tbody>
</table>

**Type of diabetes & Age**

- **Type 1**: 1 (33.3)
- **Type 2**: 2 (66.7)
- **Other Type**: 0 (0.0)

**Number of patients**: N (%)

- **≤15**: 1 (2.2)
- **15 - 25**: 100 (5.2)
- **25 - 50**: 2 (0.0)
- **50 - 65**: 4 (0.4)
- **65 - 80**: 1 (0.2)
- **≥80**: 0 (0.0)

**New statistical report**: For each new statistical report, it is checking the quality of the data submitted to meet the rigorous of the EUBIROD software. Pre-processing data for the statistical engine, triggering functions of the statistical engine, browsing statistical outputs, loading statistical objects into a central database, triggering functions of the central engine, transferring statistical objects to the central server. When editing the configuration of the input data sources, the user may choose among three different source types: a database table, a CSV file, or an XML file (BIRO format).

**Central engine** for global reports allows configuring and running a global statistical analysis on multiple statistical objects and browsing the results obtained. The configuration panel asks the user to specify the year(s) of interest for analysis and the database to be used as a basis for calculations.

**Communication** software for data transmission and exchange follows specifications advised by privacy assessment to securely transmit the CSV folder including statistical objects from the local to the Central BIRO system. Web services have been used to comply with basic requirements, including availability of an open platform-independent standard, XML support, usability over Internet protocols, open source implementation and comprehensive security support. The core technology used for communication for their compliance with standards set by the open World Wide Web consortium: SOAP (Simple Object Access Protocol) for messaging, HTTP (Hypertext Transfer Protocol) for Internet transport and XML (eXtensible Markup Language) together with its security extensions XMLSec (encryption) and XMLSig (digital signatures). Apache Axis 2, together with Apache Rampart provided by Java 2 Enterprise Edition, were chosen for pilot development and configuration of sending and receiving applications.

**Fields mapping configuration** to configure mapping between EUBIROD fields and local fields. The minimum dataset defined contains 68 data items (47 defining clinical data; 21 specifying geographical demography). Each item contains a standardised definition and, where necessary, translational mappings or calculations. For each of these data items, considerable metadata has been accumulated describing the characteristics of the data within partner sites, including quality, completeness, reliability and validity.

**EUBIROD Technology**: The adoption of the technology developed within BIRO project to new applications in the data processing chain (for example, detects unacceptable values as well as inconsistencies among values within the same record). For local users EUBIROD is an application that displays data from one or more databases. The application uses the Hibernate framework as the persistence layer for retrieving and storing plain old Java objects (POJOs) to a central standard relational database. Hibernate is framework that provides tools for object relational mapping (ORM). The configuration file contains information about the database connection, resource mappings, and other connection properties.

The EUBIROD system is substantially more efficient than the BIRO system. The main screen EUBIROD box GUI (Fig. 1) provides a detailed illustration the major work areas in a graphical user interface with a few mouse clicks. Each of EUBIROD technology functions contains a number of individual sub-functions, which are serviced by the specific technologies that configure and run adaptor, configure EUBIROD database, configure and run database manager, configure and run statistical engine and configure and run EUBIROD communicator. The EUBIROD system allows transporting different databases towards a structured data format (XML), through cleaning and standardization of the original datasets, to finally submit EUBIROD data to the statistical engine which delivers EUBIROD reports successfully.

**Setup panel** shows the current working directory and it consists in install some prerequisite software: R statistical software (version 2.8.0 recommended which can be downloaded from http://www.r-project.org), install the latest version of Java SE (JDK) from http://java.sun.com/javase/downloads/index.jsp (all Java versions since 1.6.0_6 are guaranteed to work), install MiKTeX 2.7 (can downloaded it from http://miktex.org), install Apache Ant from http://ant.apache.org/ (all versions since 1.6.5 are guaranteed to work). The update BIROBox setup file (EUBIROD version) is a self extracting file, assuring automatically installation and configuration the above mentioned software.

**Database engine** panel most of the work is specifically data processing and includes: (a) “adaptor” reads local data from XML files, CSV files or database tables, maps them to EUBIROD standard format and produce XML files representing each patient separately (data can be loaded directly into the BIRO database without an intermediate step); (b) “database manager” reads the XML files and import them into BIRO PostgreSQL database; and (c) “statistical engine” extract data from BIRO database and produces statistical indicators directly from CSV files, produces HTM formatted XML, through cleaning and standardization of the data, the statistical engine groups episode data, based on the value of the variable used as a “sub data source”, to produce stratified indicators for each level of that variable. By selecting the “Browse” button in the Statistical Engine panel, the BIROBox displays the Statistical Engine browser, i.e. a window listing all the statistical reports ever produced.

**Central engine** for global reports allows configuring and running a global statistical analysis on multiple statistical objects and browsing the results obtained. The configuration panel asks the user to specify the year(s) of interest for analysis and the database to be used as a basis for calculations.

**Communication** software for data transmission and exchange follows specifications advised by privacy assessment to securely transmit the CSV folder including statistical objects from the local to the Central BIRO system. Web services have been used to comply with basic requirements, including availability of an open platform-independent standard, XML support, usability over Internet protocols, open source implementation and comprehensive security support. The core technology used for communication for their compliance with standards set by the open World Wide Web consortium: SOAP (Simple Object Access Protocol) for messaging, HTTP (Hypertext Transfer Protocol) for Internet transport and XML (eXtensible Markup Language) together with its security extensions XMLSec (encryption) and XMLSig (digital signatures). Apache Axis 2, together with Apache Rampart provided by Java 2 Enterprise Edition, were chosen for pilot development and configuration of sending and receiving applications.

**Fields mapping configuration** to configure mapping between EUBIROD fields and local fields. The minimum dataset defined contains 68 data items (47 defining clinical data; 21 specifying geographical demography). Each item contains a standardised definition and, where necessary, translational mappings or calculations. For each of these data items, considerable metadata has been accumulated describing the characteristics of the data within partner sites, including quality, completeness, reliability and validity.
In this paper, we implemented the process steps for set-up and execution of the EUBIROD software tools (EUBIROD box GUI) to create and deliver structured Diabesity data in XML format (a standard format for the exchange of aggregate data) from structured local data sources and to further query and process these data with EUBIROD statistical reporting engines.

Statistical analysis: For advanced statistical analysis data were analysed using EUBIROD statistical computing environment (statistical engine) based on the open-source statistical language R. The C-M-H Chi-Squared test transformation was applied.

RESULTS

Data is going to be a differentiating factor in the diabesity space. After exclusion records with errors with EUBIROD pre-defined criteria, 1797 people were eligible for data analysis. Underweight with BMI <18.5 kg/m² was in a smaller proportion of people with diabetes Type 2 newly diagnosed, 11 of 1763 (0.6%). Only 267 of 1763 (15.1%) in Type 2 newly diagnosed diabetes had normal BMI on range [18.5–25 kg/m²). Overweight is highly prevalent in Type 2 as is shown on Table 2: 557 (31.6%) of 1763 (98.1%) diabetes in newly diagnosed patients had abnormal BMI on range (25–30 kg/m²). Obesity is highly prevalent in Type 2 as is shown on Table 2: 928 (52.6%) of 1763 (98.1%) diabetes in newly diagnosed patients had abnormal BMI above 30 kg/m².

Also, obesity is highly prevalent in Type 2 as is shown on table 2, 928 (52.6%) of 1763 (98.1%) diabetes in newly diagnosed patients had abnormal BMI above 30 kg/m². Our results are based on a technology developed specifically within a project for public health.

<table>
<thead>
<tr>
<th>BMI kg/m²</th>
<th>Type 1 (%)</th>
<th>Type 2 (%)</th>
<th>Other Type (%)</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;18.5</td>
<td>4 (19.0)</td>
<td>11 (0.6)</td>
<td>0 (0.0)</td>
<td>15 (0.8)</td>
</tr>
<tr>
<td>[18.5–25)</td>
<td>11 (52.4)</td>
<td>267 (15.1)</td>
<td>9 (69.2)</td>
<td>287 (16.0)</td>
</tr>
<tr>
<td>[25–30)</td>
<td>3 (14.3)</td>
<td>557 (31.6)</td>
<td>0 (0.0)</td>
<td>560 (31.2)</td>
</tr>
<tr>
<td>≥30</td>
<td>3 (14.3)</td>
<td>928 (52.6)</td>
<td>4 (30.8)</td>
<td>935 (52.0)</td>
</tr>
<tr>
<td>Total</td>
<td>21 (1.2)</td>
<td>1763 (98.1)</td>
<td>13 (0.7)</td>
<td>1797 (100.0)</td>
</tr>
</tbody>
</table>

Table 2

BMI * Type of Diabetes
Results from our collaboration study suggest some implications to help and motivate patients with obesity to recognize the beneficial effects of diet and physical activity on the metabolic control in the prevention of pre-diabetes/diabetes and the metabolic syndrome and on the associated psychological burden.

What we discovered, as is shown on Table 3: BMI * Gender, only 145 of 878 (16.5%) male and only 122 of 885 (13.8%) in Type 2 newly diagnosed diabetes had normal BMI on range \(18.5 \leq \text{BMI} \leq 25\) kg/m\(^2\). Figure 2 shows BMI for male and female for underweight BMI < 18.5 kg/m\(^2\), normal-weight (BMI 18.5–25 kg/m\(^2\)), overweight (BMI 25–30 kg/m\(^2\)) and obese (BMI > 30 kg/m\(^2\)) groups.

**DISCUSSION**

Principal findings EUBIROD presents a novel, efficient and easy to use technology to manage local data and obtain statistical results on a number of diabetes care indicators and how future policy measures in these areas might be directed to benefit prevention, intervention and overall patient care at diabetes centres, regional, national and Europe level. Our global EUBIROD statistical report (automatically generated) was given as an exhaustive PDF document of 363 pages and as html pages, with tables and graphics related to various diabetes outcome indicators.

On this paper we used EUBIROD technology specifically to assess the relationship between obesity and diabetes. These data confirm that Type 2 diabetes, associated with obesity is today the most common form of diabetes. Nowadays obesity can be usually treated with in-patient nutritional, physical, endocrinological and psychological based treatments, pharmacological treatments and also bariatric surgery. Many problems are due to the high costs of this procedures overall in a public health strategy. Cost-effective approaches (phone, mail or distance monitoring and treatments) that can reach a broad population of individuals are needed and have to be better evaluated overall if we consider the out-patient treatment or the follow-up steps of the intervention. To tackle diabesity problem through cost-effective approaches a high level of compliance and enduring care is needed.

Strengths and weakness of the study Our study demonstrates that it is perfect feasible the open distance collaboration, based on a new technology, between two partners, a diabetes centre (Institute “N. Paulescu”) and a technical partner (Telemedica Consulting, Bucharest) to develop studies using European standardized data definitions for monitoring of diabetes complications and health care outcomes in diabetes. The production of a standard dataset as a project, EUBIROD was concerned with the collaborative creation of documents and software tools in order to extract and share data from multiple sources. The reliability of this novel technology is based on
extensive routines for data quality check to filter all data inconsistencies before handling all data to the statistical engine. Results of the quality check were summarized into a small report containing a quality evaluation and the detailed list of problems encountered. Such a report was used for a self-evaluation made by the users in terms of proper data collection methods, data accuracy, and correct usage of the EUBIROD system. The EUBIROD outcome indicators, based on data recorded (at least one measurement in 12 months), include process quality outcomes (individual level) e.g. BP, lipids, HbA1c, BMI, smoking, treatment (glucose lowering treatment) management (visit frequency); outcome quality – intermediate outcomes, e.g. HbA1c > 9.0 % (poor control), subjects with most recent HbA1c > 7.5 %, subjects with most recent BP < 140/90 mmHg, subjects with most recent BMI > 30 kg/m², rate of current smokers among diabetes patients and outcome quality – terminal outcomes e.g. renal failure and dialysis.

There seems be substantial barriers for an extensive implementation of a common approach e.g. the one advocated by EUBIROD. This process requires the collaboration of highly skilled technical experts who understand both the informatics technology used to implement EUBIROD software tools as well as the medical context in which these tools were need to operate. We report in this document the results obtained following the process steps used in installing the EUBIROD technology (Box GUI) and the use of this tool in creating and delivering structured data from local data sources that can be queried and processed by EUBIROD statistical and EUBIROD reports programs. Results are fed back to local diabetes centres in a benchmarking exercise, to inform local care providers about their services, and to assist local quality development.

**EUBIROD in relation with other projects**

EUBIROD was a continuation of the BIRO project and represents the practical way to implement the excellent results of this project at the continental level. BIRO – “Best Information through Regional Outcomes” – was part of a Public Health Project funded by the European Commission, DG-SANCO 2005, and ran between November 2005 and October 2008 with an extension by May 2009 (DG-SANCO approval). Formally, it was a “Shared Evidence-Based: Diabetes Information System to Support European Health Policy” within DG-SANCO 2005 programme managed by DG-SANCO, and was coordinated from Perugia University, Italy. More details about the formal structure of the project can be found on the BIRO web site – www.biro-project.eu. BIRO developed a new method to realize a transnational information system linking heterogeneous diabetes registers. Simion Pruna, Telemedica Consulting, Romania has initiated the BIRO project with Massimo Massi Benedetti, Perugia University, Italy, based on our extensive experience for the systematic data collection and monitoring of diabetes complications and health outcomes across Europe. We had this initiative since 2002 aiming proper technology development, through a sound concept, which was expressed on the “DiabData” project materialized as an “Expressions of Interest (EoI) http://www.telemed.ro/DiabData_EOI.pdf to identify research actions ready for specific programme topics as a basis for the preparation of work programmes for the 6th framework programme for research”14, 15. For drafting of current paper we looked back what we had written on the above mentioned EoI: “decision makers need concise, reliable information about current background situation of diabetes care at local, national, regional or European level. What has happened at most medical organisations is current data only. Data often are fragmented in separate operational systems such as accounting or payroll so that different managers make decisions from incomplete knowledge bases. Because policy-makers are required to make decisions and to allocate resources which are likely to have important and lasting consequences for many million of people, the high amount of data offered by the DiabData warehousing, by integrating key diabetes data from many sources in a form that is consistent, reliable, and easy available for reporting, is a necessity”. The objectives of the DiabData project were: a) to address the fragmentation of European research of data-collection; b) to aggregate clinical data stored in disparate legacy systems; c) to evaluate health status of clinical care at both the organizational level and clinical interaction; d) to decrease diabetes mortality and diabetes morbidity. This superior database enables the policy makers to identify the needs to improve the quality of life of a growing number of European citizens. With distinctive features and functionalities, the BIRO project produced technique and tools, based on top technologies, to create a universal integration
platform of standardized structured clinical diabetes data. One crucial element to understand the background situation of diabetes care at national, regional or European level was building a high-quality and massive database about outcomes and resource utilization in diabetes. Through EUBIROD technology the data will be collected and gradual integrated from a variety of primary and secondary data sources using state-of-art technology of data-collection that could represent a broad array of database models.

Children and young patients with obesity

According EUCID project results (figure 3a and figure 3b) the problem of childhood obesity is of particular relevance in our country, leading to diabetes or pre-diabetes impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) in early adulthood. Particularly in obese subjects, the initial metabolic defect produces higher-than-normal post-prandial glucose levels, frequently missed at routine biochemical testing.

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Fig 3. (A and B) EUCID project - crude and standardised Incidence by the age structure of the European population (IARC-1976) of diabetes amongst children 0-14 years old in the EU.
The EUBIROD technology impact for children and young patients with obesity may represent true milestones in the field of diabesity research and could be on the efficacy of the care service approach that will use digital support, electronic communication and computer based support at research for advancing knowledge for diabetes and obesity care. Future large-scale randomized controlled trials including psychological variables (psychometric batteries with clinical scales, quality of life evaluation, personality inventories, neuropsychological tests, and clinical structured interview), nutritional variables (eating behaviors, diet structure) and medical parameters (body mass index, physiological variables) are needed to address diabesity. Healthy diet and physical activity have proved effective to reduce the incidence of diabetes in populations at risk, improve the metabolic profile and cardiorespiratory fitness in subjects with diabesity and reduce the cardiovascular risk associated with the metabolic syndrome.

The paper addresses the management of obesity and diabetes in practical terms useful to clinicians with an interest in diabetes, both in primary and secondary care, general practitioners, paediatricians, endocrinologists and nutritionists, as well as to students and researchers interested in obesity. To provide reliable and comparable data to various reporting tools and statistical applications, EUBIROD technology faces many problems. These include the bringing together of data with different patterns, structures and syntax, and allowing users to access information located in different places in a uniform manner. In this process, data needs to be understood, integrated and put into a uniform representation. In this respect the BIRO core dataset has been defined (work package 3), after the analysis of existing datasets used by BIRO partners. The objective of this work package was “to identify consistencies and inconsistencies with the recording of data items and to create a universal definition for each of the items comprising the dataset”.

The EUBIROD technology is needed in order to be able to monitor diabetes care and evaluate the necessary measures and policies according to the International protocols, guidelines/standard operating procedures and indicators and to measure, communicate, inform and Support European Health Policy’ decisions and choices based on clinical guidance. The data collected aim to provide insight of the quality of health care process, to improve efficiency, and to identify the causes of problems that may appear during the diabetes care process. The next challenge will be the implementation of live reporting from EHCR data collection systems, databases and data warehouses, enabling real-time access to real-time data. An interactive interface allows users to query the database and generate reports.

CONCLUSIONS AND FUTURE PROSPECTS

This new technology is based on several components that automatically generate local statistical reports and safely collect aggregate data to produce international reports of diabetes indicators, using the same European standardized data definitions, statistical routines and transmission formats. The EUBIROD technology is available as Open Source system (free software) and supports gathering diabetes data (data integration, data storage and data usage) from various local sources. A number of technical, deployment and sociocultural experiences will be gathered throughout the EUBIROD technology. We hope that these experiences can be transferred to a wider community for the benefit of patients and citizens in Romania. We also believe that many of the EUBIROD applications can be, from the technical point of view, relatively easy transformed into many other diabetes centers in Romania. This EUBIROD project was supported by DG-SANCO of the European Commission, to explore and look for ways in which data could be put to better use and to support executive decision-making through detailed analysis and enhanced quality of diabetes care.

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We are grateful to all project participants who gave their time and efforts to the novel EUBIROD technology development, all those involved in the conception and design, in the data interpretation and in the critical revision within technology transfer into practice. It is a pleasure to acknowledge the contribution of Massimo Massi Benedetti, Fabrizio Carinci, Valentina Baglioni, Joseph Azzopardi, George Olympios, Vivie Traynor, Scott Cunningham, Peter Beck and Fred Storms for fruitful discussions during the EUBIROD project partnership.

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