SCREENING FOR DIABETIC HYPERTENSION IN NEWLY DIAGNOSED TYPE 2 DIABETES USING A NEW TECHNOLOGY THAT CARRIES OUT IN MINUTES AGREGATED DATA ANALYSIS


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There is a definite need for the fast and efficient data analysis procedure in epidemiological studies. Our new technology “European Best Information through Regional Outcomes in Diabetics (EUBIROD)” based on a novel and easy to use open source software package is addressing this issue. We applied it to identify the risk factors of hypertension in newly diagnosed Type 2 diabetes. Data were analysed automatically and can have information pushed to system on a regular basis (biannually or annually). The new system can produces outcomes (tables, charts and statistics) for more than 50 indicators (European Diabetes Indicators) by various reporting tools and statistical applications placed on a central-server. After exclusion records with errors with EUBIROD pre-defined criteria, we analysed SBP and DBP on baseline data of 2285 newly diagnosed Type 2 diabetes patients in 2010, n=1,158 (50.7%) women, aged 59 ± 13.6 yrs. and n=1,127 (49.3%) men, aged 54 ± 13.9 yrs. They were recruited by randomly selected physicians from National Institute of Diabetes, Bucharest, Romania. The C-M-H Chi-Squared test transformation was applied. In Type 2 newly diagnosed diabetes, only 645 of 2285 (28.2%) had normal SBP (<130 mmHg), and only 888 of 2285 (38.9%) had normal DBP (<80 mmHg), whereas 1640 of 2285 (71.8%) had elevated SBP (SBP ≥ 130 mmHg) and 1397 of 2285 (61.1%) had elevated DBP (DBP ≥ 80 mmHg). Hypertension is highly prevalent in the very elderly. The numbers of records for SBP/DBP and age band, normal and abnormal, are summarized in Table below (created through EUBIROD package). The EUBIROD outcome provides a cost effective solution to data analysis issues by using built-in advanced statistical approaches to work with aggregated data. SBP and DBP in huge majority of the type 2 newly diagnosed is elevated. Early detection of cardiac insufficiency episodes is allowing practitioners to follow up their heart impaired patients to better adjust their treatment in a prompt and optimal way.

Key words: Hypertension, Newly Diagnosed Diabetes, Type 2 diabetes, BIRO software packages, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP).

INTRODUCTION

Diabetes is a serious chronic disease that occurs when the pancreas does not produce enough insulin to maintain glucose homeostasis relative to the physiological demand. Many studies of Type 2 (non-insulin-dependent) diabetes mellitus assume that the diabetes condition is homogeneous and clearly defined. There are, however, several problems with these assumptions. It is a metabolic disease with completely different aetiologies: type 1 diabetes, characterized by autoimmune destruction of the beta cells, resulting in an absolute beta cell deficiency or type 2 diabetes, results from the body’s
unproductive use of insulin caused by a relative beta cell deficiency resulting from peripheral insulin resistance.1

A high glucose level may cause damage in several parts of the body, especially heart, blood vessels, nerves, eyes, kidneys, and feet. Several studies show that a major cost component is due to the care of diabetic complications, not to the treatment of the illness itself; in particular, drug costs represent a relatively small proportion of such treatment cost. Diabetes can also produce high blood pressure and hardening of arteries.3,4 Analysis of the data evidence suggested that low serum potassium concentrations or hypokalaemia induced by the intake of diuretics are associated with incident diabetes and increased risk for diabetes in persons with hypertension.5 Hypertension is an important clinical characteristic in management and treatment in diabetes for patients with chronic cardiovascular diseases in different scenarios of their daily life. It is a known risk factor for cardiovascular diseases, including heart disease and stroke. Systolic Blood pressure (SBP) has an important role in diabetic mortality.6 The effect of glycaemic variability (GV) on cardiovascular risk has not been fully clarified in type 2 diabetes. A recent study shows that an impaired GV and BP variability is associated with endothelial and cardiovascular damage in short-term diabetic patients with optimal metabolic control. Also, oxidative stress is the only independent predictor of increased left ventricular mass index (LVMI) and correlates with glucose and BP variability.7 Gender differences in hypertension control have not been explored fully because the vast majority of software development tools used in the diabetes sector today do not inherently support data exchange mechanisms.9, 10, 11 The aim of the EU DG-SANCO project EUBIROD was to unidirectional migration of data from various local data sources to regional data warehouses (BIRO aggregated data) to produce “local” reports of standardized indicators and from there to the central Shared European Diabetes Information System (SEDIS), where data analysis is performed to obtain internationally comparable.

<table>
<thead>
<tr>
<th>Age Yrs.</th>
<th>Gender</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Male (%)</td>
</tr>
<tr>
<td>&lt;15</td>
<td></td>
<td>2 (0.2)</td>
</tr>
<tr>
<td>[15–25]</td>
<td></td>
<td>3 (0.3)</td>
</tr>
<tr>
<td>[25–50]</td>
<td></td>
<td>272 (24.1)</td>
</tr>
<tr>
<td>[50–65]</td>
<td></td>
<td>535 (47.5)</td>
</tr>
<tr>
<td>[65–80]</td>
<td></td>
<td>284 (25.2)</td>
</tr>
<tr>
<td>≥80</td>
<td></td>
<td>31 (2.8)</td>
</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td>1127 (49.3)</td>
</tr>
</tbody>
</table>

Fig. 1. Barplot: Age * Gender.
health indicators (The BIRO Project, deliverable D6.2), The EUBIROD Project, deliverable D7.1, (Simion Pruna (Romania), Joseph Azzopardi (Malta), G.Olympios, V. Traynor and Andriana Evripidou (Cyprus)BIRO Technology Transfer Deliverable 12.2). This article will summarize the evidence for the EUBIROD criteria that imply analysis of isolated systolic hypertension and isolated diastolic hypertension, which try to classify hypertension into stages, based on levels of SBP and DBP. Hypertension is highly prevalent in the very elderly and is an important clinical characteristic in management and treatment in diabetes. EUBIROD presents a novel, cost effective and easy to use technology to this problem. The objective is for participating Diabetes centers to collect audit data for regional analysis, and through coordination of the work through the Telemedica Consulting, to gather national diabetes statistics from data collected at participating clinics. The anonymised records were collected on Excel spreadsheet, and a BIRO data set used for data exchange.

**MATERIALS AND METHODS**

The numbers of records, their male/female split by age bands is given as Table 1 created through EUBIROD package. The numbers of records and numbers of patients with an identified diabetes type and age band is given as Table 2. Patients were from Ambulatory Centre of Diabetes, Inst. “N. Paulescu”, located in Bucharest, Romania. Systolic blood pressure (SBP) and Diastolic blood pressure (DBP) were items (variables) used on this study. The technology developed in EUBIROD project is available Open Source and supports gathering diabetes data (data integration, data storage and data usage) from various local sources. For local users EUBIROD is a web application that displays data from a database (data table or CSV file as data input) to manage local data and obtain statistical results with BIRO statistical reporting engines. Missing values, values with wrong format and out of range values were detected automatically by the software package and removed.

**EUBIROD Technology**: For local users EUBIROD system is a cross-platform application powered by Linux Ubuntu that displays data from a database (a database table or CSV file as data input) to manage local data and obtain statistical results of diabetes indicators, which can be used to develop recommendations for policy makers (D5_3_Database_Engine).

A full EUBIROD comprehensive graphical user interface functional description, reaching significant improvements by the third year and then continuing until the project close-up, is available elsewhere [Vasile Cristescu, Constantin Ionescu-Tirgoviste and Simion Pruna, (2012)]. One of the substantial improvements was the first adaptor version in matter of usability. The old database adaptor could be executed from the console connection (Figure 2) and it required some programming proficiency to configure the tool through a plain text file and therefore, usability and clarity suffered because of this.

For the new EUBIROD adaptor based on the complete database connection configuration tool GUI (Figure 3), no longer needs to understand and to write script commands. It is much easier on the eyes and much easier to use. The EUBIROD application (routines and the graphical user interface) can be used to navigate and examine EU diabetes metadata, based on common metadata vocabulary (the common dataset) and that can have information pushed to it on a regular basis (biannually or annually) for subsequent analysis by various reporting tools and statistical applications placed on the EUBIROD central server. Software elements that were developed in EUBIROD project support the use of this information by assisting in the extraction, analysis, and reporting of diabetes information.

The main screen merge table source configuration GUI (Figure 3) provides an illustration the five major work areas in a graphical user interface with a few mouse clicks: (a) BIRO Adaptor, (b) BIRO database, and (c) BIRO Communication software. Each of these contains a number of individual functions, which are serviced by the specific technologies that configure and run adaptor, configure BIRO database, configure and run database manager, configure and run statistical engine and configure and run BIRO communicator. In this report, we successfully implemented the process steps for set-up and execution of the BIRO software tools (BIRO box GUI) to create and deliver structured 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 BIRO statistical reporting engines.

### Table 2

<table>
<thead>
<tr>
<th>Type of diabetes</th>
<th>Age (Yrs.)</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;15</td>
<td>15–25 (%)</td>
</tr>
<tr>
<td>Type 2</td>
<td>3 (100.0)</td>
<td>5 (100.0)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>3 (0.1)</td>
<td>5 (0.2)</td>
</tr>
</tbody>
</table>

**Reading number of row to export: 4627 rows.**
**Reading 4627 values [may take a while].**
**BIRO XML: -----------------------------100% - Time: 04s**

**Document BIRO XML created.**

Fig. 2. BIRO adaptor, the export of data in the database to XML file. Once written, a local configuration file can run the tool in a completely automated way, outputting the XML file.
The production of a standard dataset

As a project, BIRO was concerned with the collaborative creation of documents and software tools in order to extract and share data from multiple sources. There seems be substantial barriers for an extensive implementation of a common approach e.g. the one advocated by BIRO. This process requires the collaboration of highly skilled technical experts who understand both the informatics technology used to implement BIRO 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 BIRO Box GUI and the use of this tool in creating and delivering structured data from semi-structured local data sources that can be queried and processed by BIRO statistical and BIRO reports programs.

Results are fed back to local districts in a benchmarking exercise, to inform local care providers about their services, and to assist local quality development.

Data Sources: Table 1 gives a breakdown of the numbers of records, their male/female split by age bands. In brief, individuals with type 2 diabetes (WHO criteria) living in Bucharest, Romania, were selected from the Bucharest Ambulatory Register. After exclusion records with errors with BIRO pre-defined criteria, 2285 people were eligible for data analysis. Table 2 gives a breakdown of the numbers of records and numbers of patients with an identified diabetes type and age band.
Statistical analysis

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

RESULTS

SBP by Age Classes

SBP on age band <15, [15–25), [25–50), [50–65), [65–80) and 80+ years, for normal SBP <130 mmHg, and abnormal SBP ≥130 mmHg is given as Table 3 (created through EUBIROD package) for type 2 diabetes. The Barplot: SBP (by Age Classes) is given in Figure 6.

How frequent is elevated SBP in Type 2 newly diagnosed diabetes?

On age range [25–50) years, 94 of 272 (34.6%) of men and 63 of 149 (42.3%) of women had normal SBP (<130 mmHg), but 178 of 272 (65.4%) of men and 86 of 149 (57.7%) of women had abnormal SBP ≥130 mmHg;

<table>
<thead>
<tr>
<th>SBP mm Hg</th>
<th>Age (Yrs.)</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;15</td>
<td>[15–25) (%)</td>
</tr>
<tr>
<td>&lt;130</td>
<td>1   (3.3)</td>
<td>4 (80.0)</td>
</tr>
<tr>
<td>≥130</td>
<td>2   (66.7)</td>
<td>1 (20.0)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>3   (0.1)</td>
<td>5 (0.2)</td>
</tr>
</tbody>
</table>

Fig. 5. Barplot: SBP * Age.
### Table 4
SBP * Gender * Age (Type of Diabetes = Type 2)

<table>
<thead>
<tr>
<th>SBP mmHg</th>
<th>&lt;15 N (%)</th>
<th>[25–50)</th>
<th>[50–65)</th>
<th>[65–80)</th>
<th>≥80 N (%)</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male (%)</td>
<td>Female (%)</td>
<td>Male (%)</td>
<td>Female (%)</td>
<td>Male (%)</td>
<td>Female (%)</td>
</tr>
<tr>
<td>&lt;130</td>
<td>0 (0.0)</td>
<td>1 (100.0)</td>
<td>3 (100.0)</td>
<td>1 (50.0)</td>
<td>94 (34.6)</td>
<td>63 (42.3)</td>
</tr>
<tr>
<td>≥130</td>
<td>2 (100.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (50.0)</td>
<td>178 (65.4)</td>
<td>86 (57.7)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>2 (0.1)</td>
<td>1 (0.0)</td>
<td>3 (0.1)</td>
<td>2 (0.1)</td>
<td>272 (11.9)</td>
<td>149 (6.5)</td>
</tr>
</tbody>
</table>

#### Fig. 6. Trellis density plot: SBP * Gender * Age (Type of Diabetes = Type 2).

### Table 5
DBP * Age

<table>
<thead>
<tr>
<th>DBP mmHg</th>
<th>&lt;15</th>
<th>[15–25) (%)</th>
<th>[25–50) (%)</th>
<th>[50–65) (%)</th>
<th>[65–80) (%)</th>
<th>≥80 (%)</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>N (%)</td>
<td></td>
</tr>
<tr>
<td>&lt;80</td>
<td>2 (66.7)</td>
<td>4 (80.0)</td>
<td>168 (39.9)</td>
<td>417 (38.0)</td>
<td>266 (39.1)</td>
<td>31 (39.2)</td>
<td>888 (38.9)</td>
</tr>
<tr>
<td>≥80</td>
<td>1 (33.3)</td>
<td>1 (20.0)</td>
<td>253 (60.1)</td>
<td>680 (62.0)</td>
<td>414 (60.9)</td>
<td>48 (60.8)</td>
<td>1397 (61.1)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>3 (0.1)</td>
<td>5 (0.2)</td>
<td>421 (18.4)</td>
<td>1097 (48.0)</td>
<td>680 (29.8)</td>
<td>79 (3.5)</td>
<td>2285 (100.0)</td>
</tr>
</tbody>
</table>
On age range [50–65) years, 151 of 535 (28.2%) of men and 148 of 562 (26.3%) of women had normal SBP (<130 mmHg), 384 of 535 (71.8%) of men and 414 of 562 (73.7%) of women had abnormal SBP ≥130 mmHg;

On age range [65–80) years, 75 of 284 (26.4%) of men and 91 of 396 (23.0%) of women had normal SBP (<130 mmHg), 209 of 284 (73.6%) of men and 305 of 396 (77.0%) of women had abnormal SBP ≥130 mmHg;

On age range 80+ years, 4 of 31 (12.9%) of men and 14 of 48 (29.2%) of women had normal SBP (<130 mmHg), 27 of 31 (87.1%) of men and 34 of 48 (70.8%) of women had abnormal SBP ≥130 mmHg;

These results indicate that there was no significant differences in SBP abnormal percentages between males and females for all age classes. As shown in the Table 4, hypertension is highly prevalent starting in the very elderly patients, both male and female.

DBP by Age Classes

DBP on age band <15, [15–25), [25–50), [50–65), [65–80) and 80 + years, for normal DBP <80 mmHg, and abnormal DBP ≥80 mmHg is given as Table 5 (created through EUBIROD package) for type 2 diabetes. The Barplot: DBP (by Age Classes) is given in Figure 7.

How frequent is elevated DBP in Type 2 newly diagnosed diabetes?

On age range [25–50) years, 102 of 272 (37.5%) of men and 66 of 149 (44.3%) of women had normal DBP (<80 mmHg), 170 of 272 (62.5%) of men and 83 of 149 (55.7%) of women had elevated DBP ≥80 mmHg;

On age range [50–65) years, 198 of 535 (37.0%) of men and 219 of 562 (39.0%) of women had normal DBP (<80 mmHg), 337 of 535 (63.0%) of men and 343 of 562 (61.0%) of women had elevated DBP ≥80 mmHg;

Table 6

<table>
<thead>
<tr>
<th>DBP mmHg</th>
<th>Gender*Age (Yrs.)</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;15</td>
<td>[15–25)</td>
</tr>
<tr>
<td>Male (%)</td>
<td>1 (50.0)</td>
<td>1 (100.0)</td>
</tr>
<tr>
<td>Female (%)</td>
<td>1 (50.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>2 (0.1)</td>
<td>1 (0.0)</td>
</tr>
</tbody>
</table>

Fig. 7. Barplot: DBP (by Age Classes).
Fig. 8. Trellis density plot: DBP * Gender * Age (Type of Diabetes = Type 2).

- On age range [65–80) years, 120 of 284 (42.3%) of men and 146 of 396 (36.9%) of women had normal DBP (<80 mmHg), 164 of 284 (57.7%) of men and 250 of 396 (63.1%) of women had elevated DBP ≥80 mmHg;
- On age range 80+ years, 8 of 31 (25.8%) of men and 23 of 48 (47.9%) of women had normal DBP (<80 mmHg), 23 of 31 (74.2%) of men and 25 of 48 (52.1%) of women had elevated DBP ≥80 mmHg;

As given in table 4, hypertension is highly prevalent in newly diagnosed Type 2 diabetes, even in the very elderly.

**DISCUSSION**

Principal findings - Our study shows that hypertension is highly prevalent in the very elderly, thus confirming data from literature. The current report shows that SBP in huge majority of the type 2 newly diagnosed are elevated which is a life-threatening deterioration frequent in heart-failure patients. These findings extend previous observations that in diabetes hypertension (defined as a blood pressure ≥140/90 mmHg) are an indicator directly related to outcomes including cardiovascular events and microvascular complications of retinopathy and progression of nephropathy. From a medical point of view, risk factors of hypertension represent a very meaningful impact to Romanian society, especially in terms of mortality, morbidity and related health economic costs. Thus, given the complexity of this kind of diseases and their associated co-morbidities, strong benefits can be obtained through the application of well-designed EUBIROD technology based on a novel software package tool for epidemiological studies and clinical trials adapted to the users’ needs. In this context, the research and technological development of EUBIROD project addressed the
strategic integration of the fields existing technical and scientific knowledge, from the medical and health policies point of view, in order to build services targeted to the user needs following diabetes onset.

**Comparison with prior studies**

There are few data assessing the prognostic importance of hypertension. Epidemiological analyses\(^{13-15}\) show that blood pressures \( \geq 120/70 \) mmHg are associated with increased cardiovascular event rates and mortality in persons with diabetes. Data collection of the relevant parameters is paramount and the key-parameter is the hypertension. Therefore, based on evidence that such data collection activities increase the early detection of the hypertension in diabetic populations a target blood pressure goal of \(<130/80 \) mmHg is reasonable if it can be safely achieved.

**How to fight SBP hypertension in Type 2, newly diagnosed diabetes?**

Hyperglycemia develops elevated BP. The data and results in this document are illustrative of the data contained in the sample of database. What we discovered was only 645 of 2285 (28.2%) in Type 2 newly diagnosed diabetes had normal SBP \(<130 \) mmHg. 1640 of 2285 (71.8%) need some intervention SBP regulation. That does not mean pharmaceutical treatment at least SBP control to address non-pharmaceutical measures. However, our findings show that in Type 2 newly diagnosed diabetes 1640 of 2285 (71.8%) had evidence of diet or medical treatment for their hypertension.

In this report we have shown the broad scope of the EUBIROD framework regarding technology transfer and the main issues surrounding evaluation and implementation by real users of the EUBIROD software tools in diabetes care locations in Romania. In a collaborative and interdisciplinary effort the EUBIROD project has to be continued for further implementation in other European countries. At national level the availability of health indicators for comparison and benchmarking at a European level must be an integral part of the national health information strategies\(^{16,17}\). For this reason, it will be vital to directly involve national health care management (e.g. Ministries of Health, Diabetes Associations, etc.) in the follow-up project EU-BIROD for further successful implementation.

Currently, the Romanian EHCR framework in diabetes appears still too heterogeneous to allow a rapid introduction of common systems and interoperable services\(^9\). The EUBIROD project not only created an infrastructure to make data from national or regional registers available for international comparison of health indicators, it also provided valuable tools and information to set up these registers.

We acknowledge that the general applicability of the EUBIROD technology has an important limitation from the statistical point of view. It is lack possibility for comparisons within and between the groups with Student’s paired and unpaired two-tailed \(t\) tests, where statistical significance should considered to be at 5% level (\(p \leq 0.05\)). This is an obvious limitation of the EUBIROD technology from statistical point of view, but it was a consequence of project consortium efforts to limit the resources necessary for statistical software development to allow the EUBIROD methods to translate easily to real-life applications.

To provide reliable and comparable data to various reporting tools and statistical applications, EUBIROD technology real-life application faces many problems. These include the bringing together of data with different patterns (available local datasets are not homogeneous, due to the different purposes and procedures in place of data collection), structures and syntax, and allowing users to access information located in different places in a uniform manner (long term longitudinal datasets may present internal inconsistencies that can be difficult to trace from the outside). In this process, data needs to be understood integrated and put into a uniform representation. In this respect the EUBIROD core dataset has been defined (work package 3), after the analysis of existing datasets used by EUBIROD 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”. This is the first time that a dataset with corresponding data definitions using an XML interface protocol has been created for a European population. As a EUBIROD partner from a new EU country, we have been tested and adapted the EUBIROD core dataset as a standard and helpful model tool in our data extraction.
CONCLUSIONS AND FUTURE PROSPECTS

In this report a description of the practical use of EUBIROD software was given. The EUBIROD outcome provides a cost effective solution to data analysis issues by using built-in advanced statistical approaches to work with aggregated data. Early detection of cardiac insufficiency episodes is allowing practitioners to follow up their heart impaired patients to better adjust their treatment in a prompt and optimal way. Health information systems in diabetes tend to be fragmented, inaccurate, cumbersome, untimely, and isolated. An EUBIROD software interactive interface allows users to query the database and generate reports. The next challenge will be the implementation of live reporting from EHCR data collection systems, databases and data warehouses. EUBIROD technology can be extended to further diseases and has even been specifically conceived and realized for that, since the entire platform may be parameterized to allow the computation of health indicators for a wide range of diseases.

ACKNOWLEDGEMENT

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REFERENCES


