THE EUBIROD REGISTRY TO UNDERSTAND SPECIFIC UNMET NEEDS IN DIABETES SUBPOPULATIONS

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HUB FOR INTERNATIONAL HEALTH RESEARCH

EUBIROD

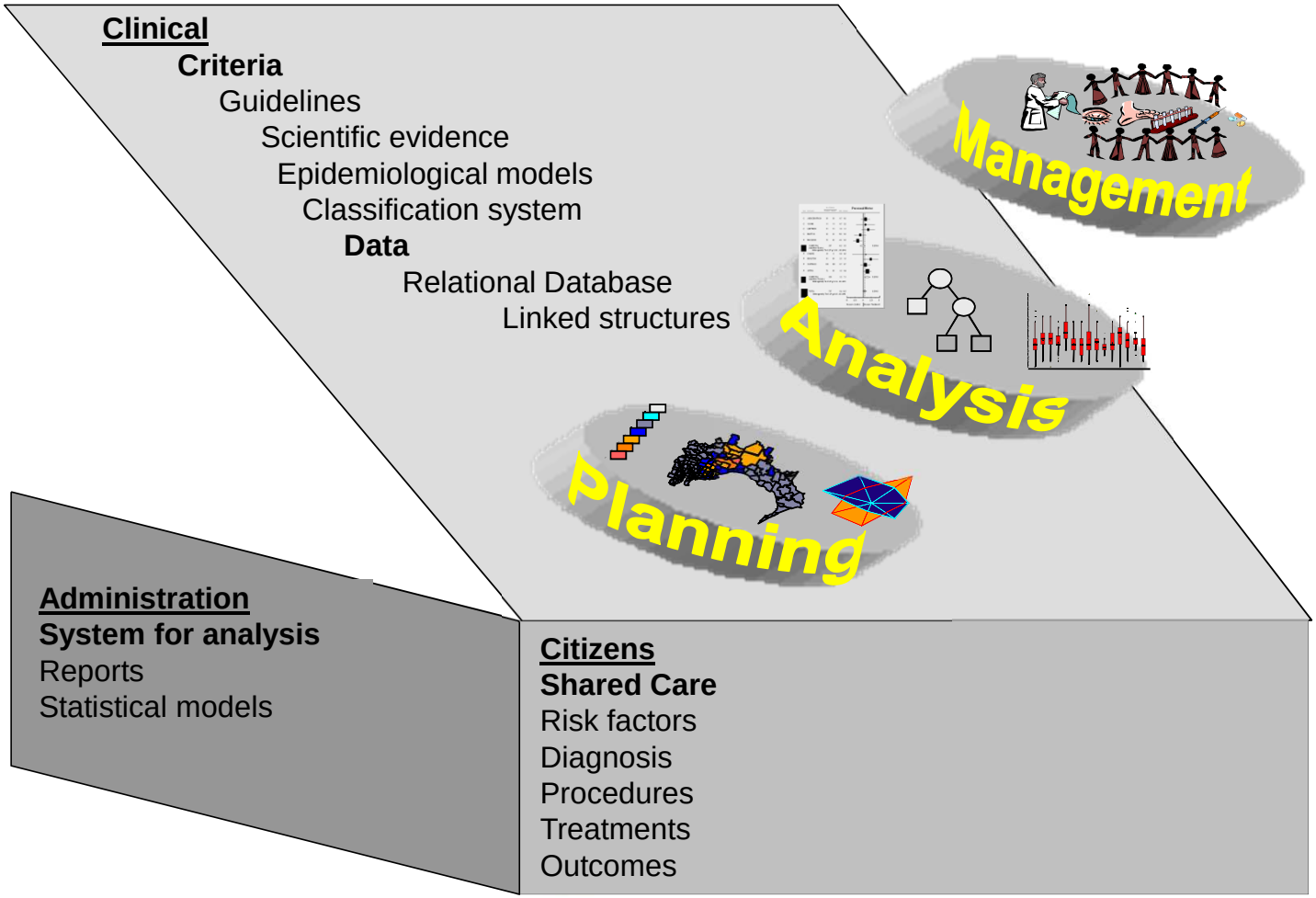
Directorate-General for Health & Consumers

Executive Agency for Health and Consumers

General Objective

"EUBIROD aims at establishing a European Diabetes Register through the extension of the BIRO network and the use of related technology."

EC Grant Agreement 2007115 EUBIROD
Brussels, 19 August 2008


Clinical
Criteria
Guidelines
Scientific evidence
Epidemiological models
Classification system
Data
Relational Database
Linked structures
Management
Analysis
Planning
Administration
System for analysis
Reports
Statistical models
Citizens
Shared Care
Risk factors
Diagnosis
Procedures
Treatments
Outcomes

MAIN ISSUES FOR SUCCESS/INSUCCESS OF REGISTRIES

- Public Health **VS** Industry driven
- Electronic Records **VS** Paper Records
- Prospective **VS** Retrospective
- Multiple Data Sources **VS** Big Brother
- Open Source **VS** Proprietary Software

- Interference with routine activities
- Work Load
- Maintenance
- Flexibility
- Scalability
- Statistical Analysis
- Time Delay in results availability
- Customisation for multiple constituencies
- **Privacy Impact**

The general objective of the project was:

to build a common European infrastructure for standardized information exchange in diabetes care, for the purpose of monitoring, updating and disseminating evidence on the application and clinical effectiveness of best practice guidelines on a regular basis

- **Open Source**
- **Public Health oriented**
- **Privacy proof by design**
- **Fully automated**
  a) **data collection**
  b) **statistical analysis**
  c) **on line report production**
- **Minimal maintenance needs**
- **Multi purpose for multiple constituencies**
- **Flexible and scalable (also to other NCDs)**

Project Consortium

1. University of Perugia (I)
2. Serectrix snc (I)
3. University of Dundee (GB)
4. Joanneum Research (A)
5. NOKLUS (N)
6. Paulescu Institute (RO)
7. University of Malta (M)
8. Republic of Cyprus (CY)
9. Sahlgrenska Institute (S)
10. University of Debrecen (H)
11. Institute of Public Health (B)
12. IDF (B)
13. Adelaide Meath Hospital (IRL)
14. CBO (NL)
15. Centre Hospitalier (LUX)
16. University of Ljubljana (SLO)
17. IMABIS Foundation (E)
18. Medical University Silesia (PL)
19. Havelhoe Hospital (D)
20. Hillerod University Hospital (DK)
21. Vuk Vrhovak University (HR)

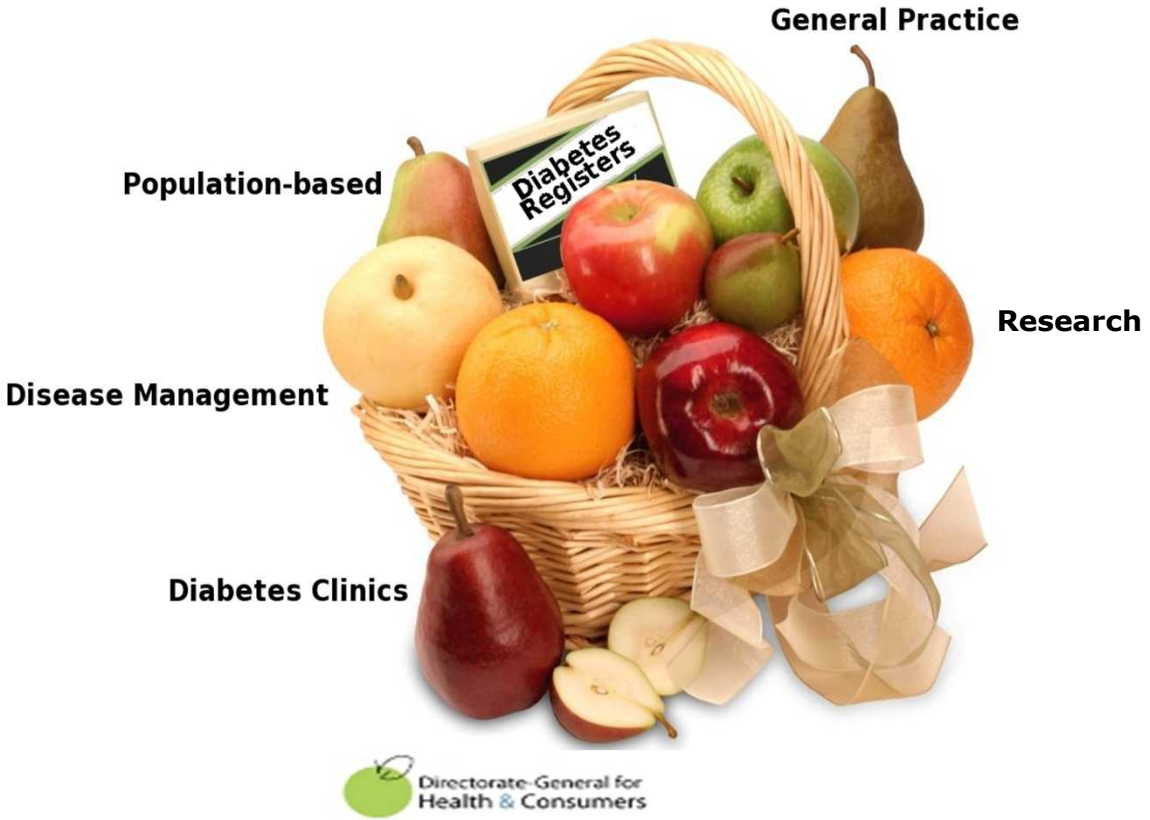
Participating Institutions:

1. Ministry of Health, Latvia
2. IDIBAPS, Spain
3. Dasman Diabetes Centre, Kuwait

BIRO 11/2005 – **9/2008**

EUBIROD 5/2009 – **3/2012**

Diabetes Registers: different fruits



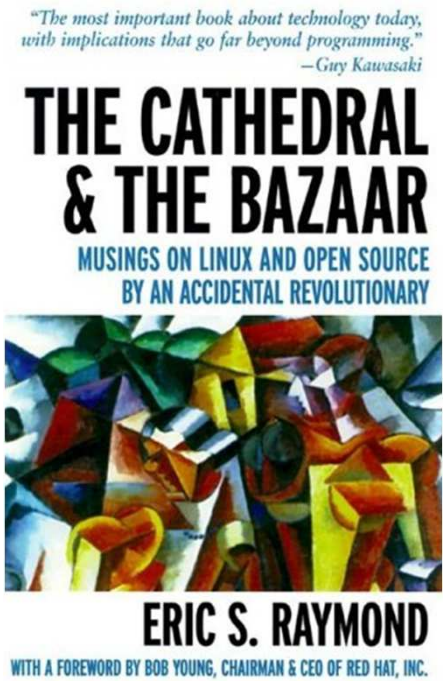
Types of Registers

“Population-based”

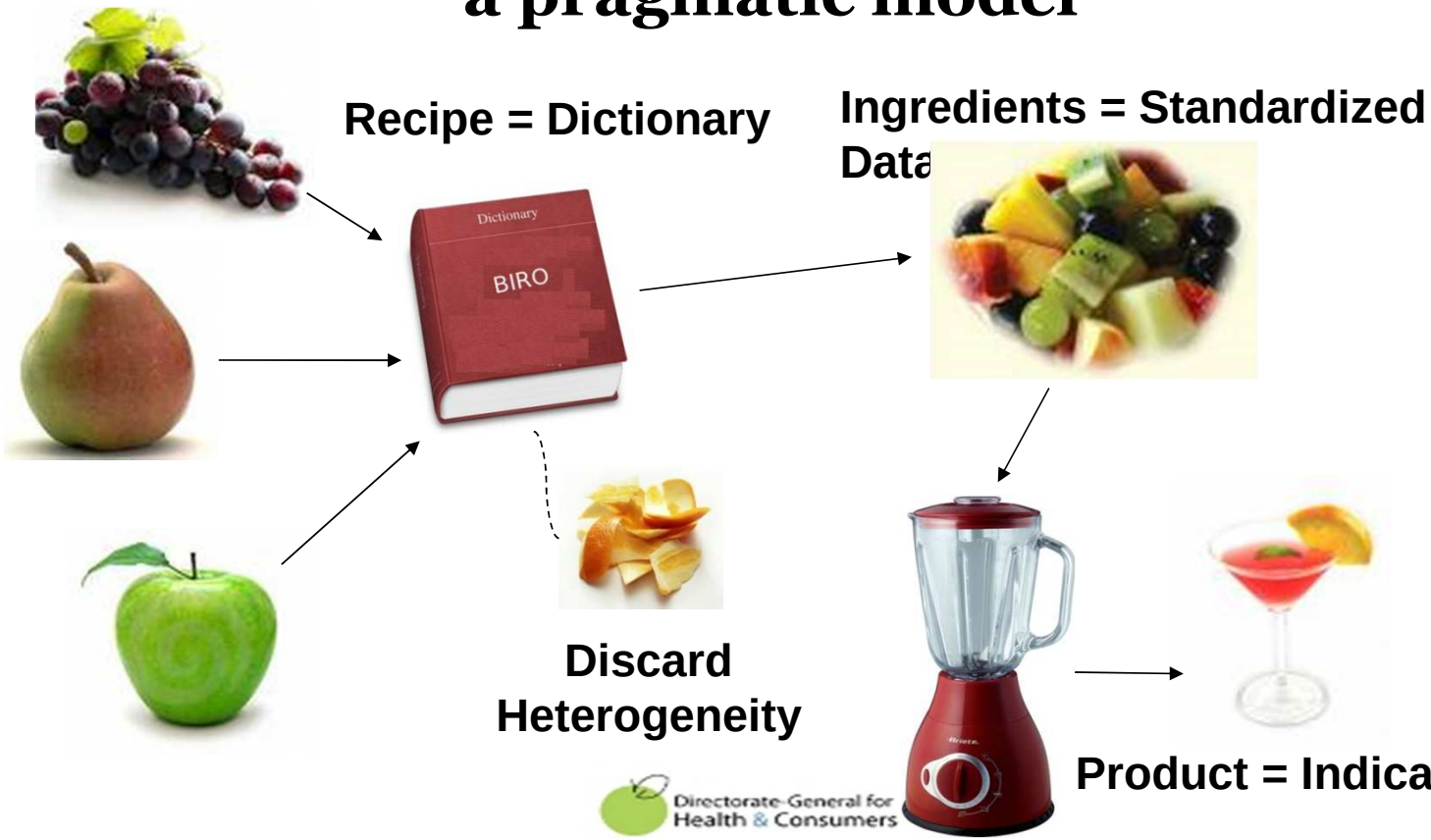
“Disease Management”

“Specialistic”

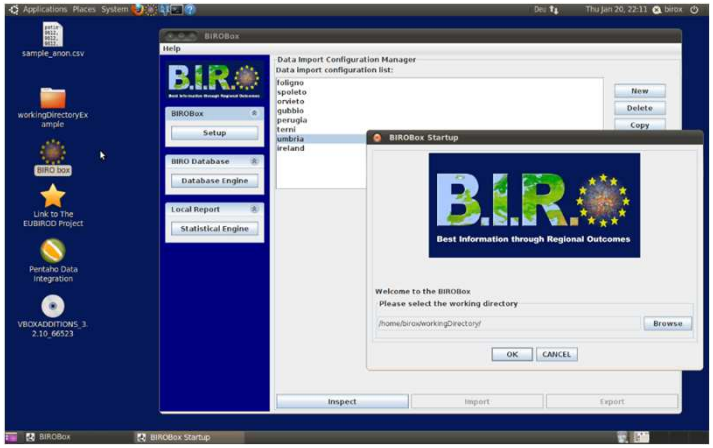
Unified model: cathedral or bazaar?



Coordination rather than unification: a pragmatic model



BIRO System Software Integration



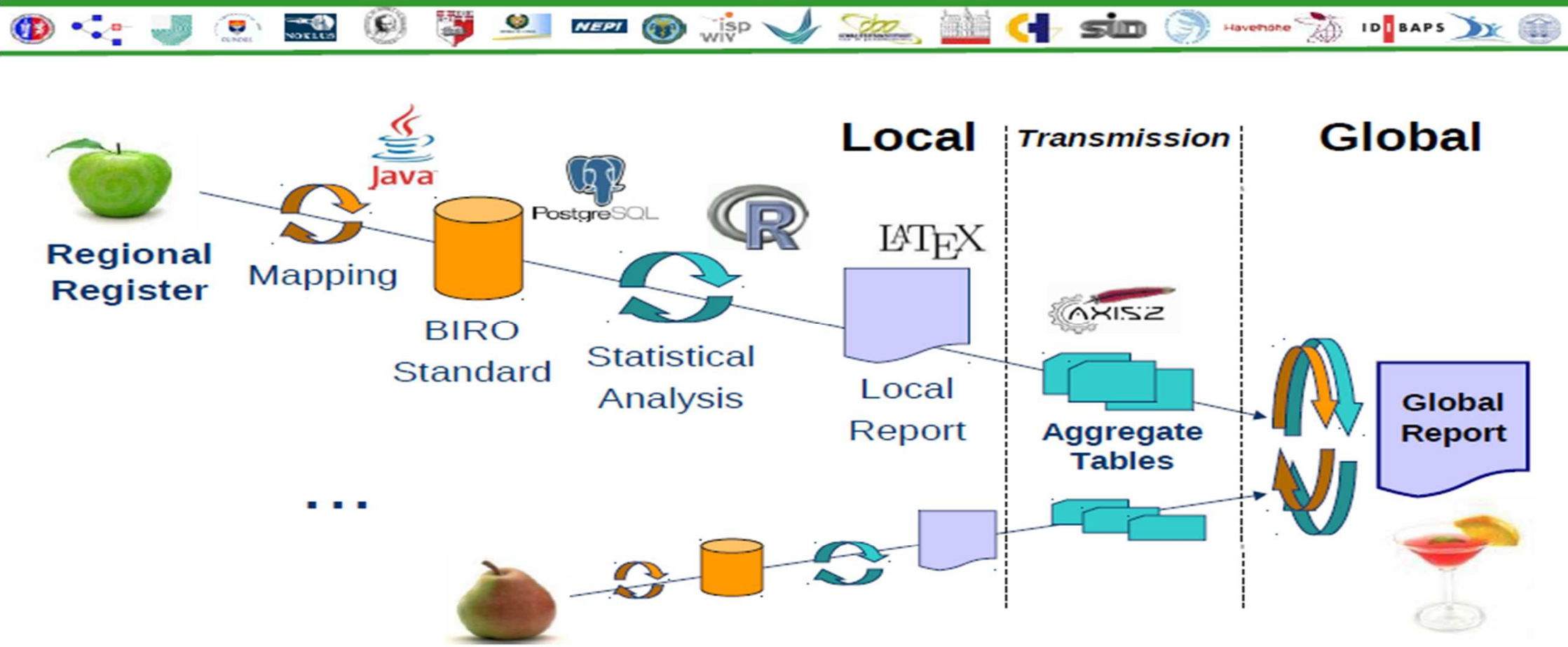
The BIRO System is an open source suite of

- integrated software tools distributed as a complete Linux operating system
- running on Virtual Machine: **BIROX**.
- Runs on any platform (Windows, Linux, MacOS) = *no need to change the setup of the local environment!*
- Privacy protection by design

BIROBox is the Graphical User Interface.

- **Database Engine** transforms local definitions into the European BIRO format and loads data in the local BIRO Database;
- **Statistical Engine** processes the local BIRO Database and computes European BIRO Indicators;
- **Communication Software** sends data to the European server;
- **Central Engine** compiles results from multiple sources

The BIRO System



BIRO Infrastructure: "Privacy by Design"

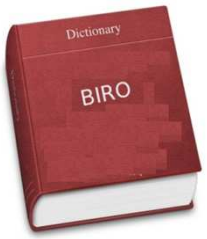
DI IORIO CT et al, J Med Ethics. 2009 Dec;35(12):753-61.

Law, ethics and medicine

Privacy impact assessment in the design of transnational public health information systems: the BIRO project

C T Di Iorio,[1] F Carinci,[1] J Azzopardi,[2] V Baglioni,[3] P Beck,[4] S Cunningham,[5] A Evripidou,[6] G Leese,[7] K F Loevaas,[8] G Olympios,[6] M Orsini Federici,[3] S Pruna,[9] P Palladino,[10] S Skeie,[8] P Taverner,[8] V Traynor,[6] M Massi Benedetti[3]

BIRO Core EU Dataset



1. ID Patient
2. ID Centre
3. Type of Diabetes
4. Sex
5. Date of Birth
6. Date of Diagnosis
7. Episode Date
8. Smoking Status
9. N.Cigarettes (x day)
10. Alcohol Intake (g/x day)
11. Weight
12. Height
13. BMI
14. Systolic Blood Pressure
15. Dyastolic Blood Pressure
16. HbA1c
17. Creatinine
18. Microalbumin
19. Total Cholesterol
20. HDL
21. Tryglicerides
22. Eye Examination
23. Retinopathy Status
24. Maculopathy Status
25. Foot Examination
26. Foot Pulses
27. Foot vibration
28. End Stage Renal Failure
29. Renal Dialysis
30. Renal Transplant
31. Stroke
32. Foot Ulceration
33. Acute Myocardial Infarction
34. Laser
35. Hypertension
36. Blindness
37. Amputation
38. Antihypertensive Medication
39. Hypoglicaemic Drug Therapy
40. Oral Drug Therapy
41. Insulin Therapy
42. Insulin Pump Therapy
43. Average Injections (x day)
44. Self monitoring
45. Diabetes Specific Education
46. Lipid Lowering Therapy
47. Anti-platelet Therapy
48. Patient enrollment in DMP for diabetes

BIRO Indicators (N=72)

http://www.biro-project.eu/documents/downloads/D14_4_BIRO_Monograph.pdf

Demographic Characteristics N=2)

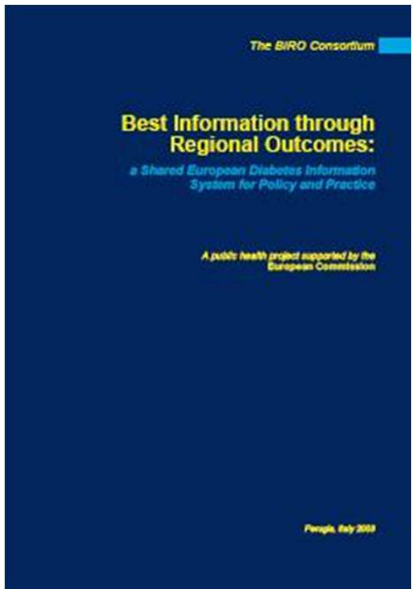
Clinical Characteristics (N=18)

Health System (N=21)

Population (N=3)

Standardized / Risk Adjusted (N=28)

- Epidemiological (N=2)
- Process (N=16)
- Intermediate Outcomes (N=7)
- Terminal Outcomes (N=3)

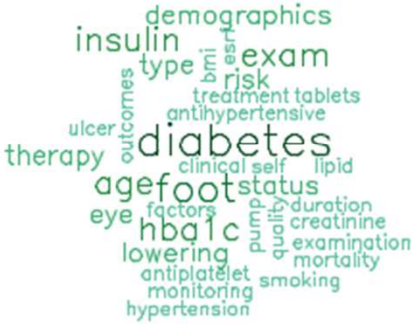


EUropean Best Information through Regional Outcomes in Diabetes

THE BIRO SYSTEM

STATISTICAL REPORT

European Diabetes Indicators



EUBIROD

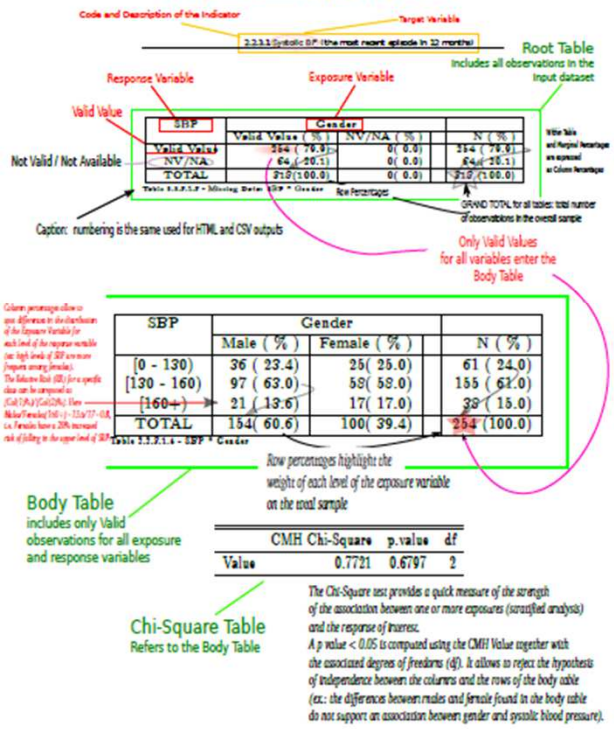
www.eubirod.eu

February 18, 2012

Executive Agency for Health and Consumers

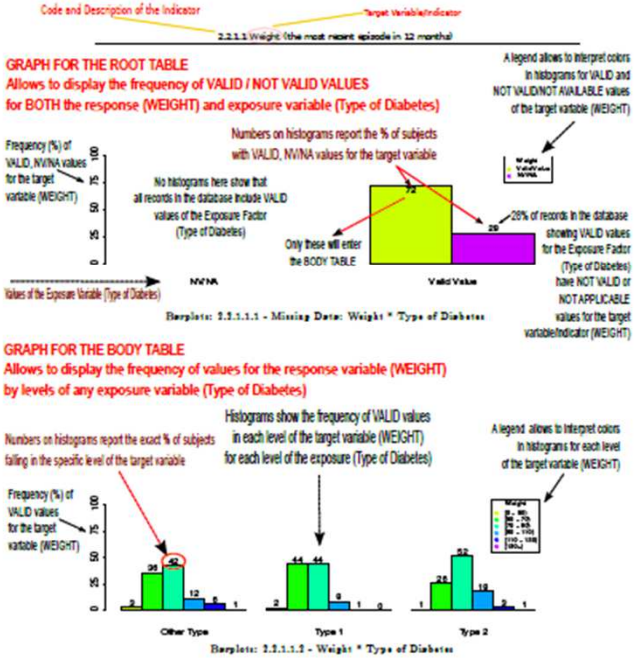
HOW TO READ THE BIRO REPORT
INTERPRETING ONE WAY TABLES

ONE WAY TABLES are used to tabulate the frequency of values for a target variable/indicator against a single exposure



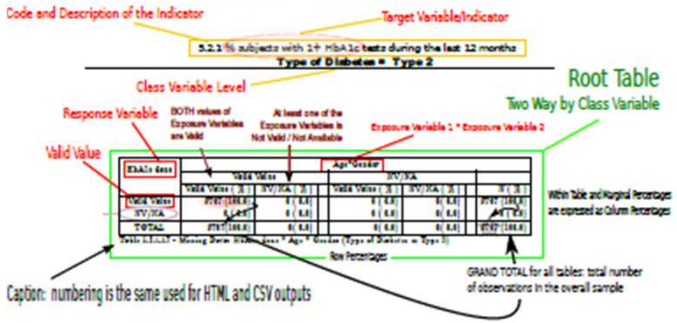
HOW TO READ THE BIRO REPORT
INTERPRETING GRAPHS FOR ONE WAY TABLES

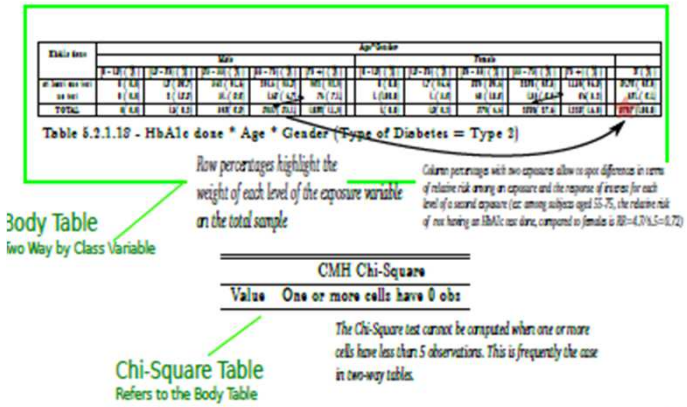
GRAPHS FOR ONE WAY TABLES are produced to provide a graphical display of the content of ONE WAY TABLES



HOW TO READ THE BIRO REPORT
INTERPRETING TWO WAY TABLES

TWO WAY TABLES are used to tabulate the frequency of values for a target variable/indicator against two exposures





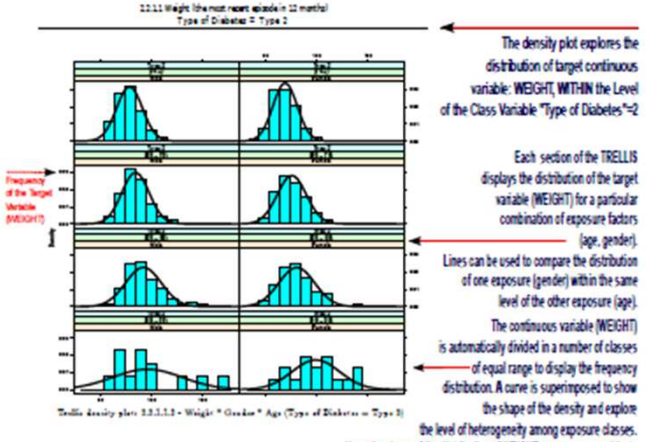
CMH Chi-Square	
Value	One or more cells have 0 obs

The Chi-Square test cannot be computed when one or more cells have less than 5 observations. This is frequently the case in two-way tables.

Chi-Square Table
Refers to the Body Table

HOW TO READ THE BIRO REPORT
TRELLIS GRAPHS FROM TWO WAY TABLES

TRELLIS GRAPHS offer a flexible graphical representation of the distribution of a target CONTINUOUS RESPONSE VARIABLE for different levels of EXPOSURE FACTORS and CLASS VARIABLES



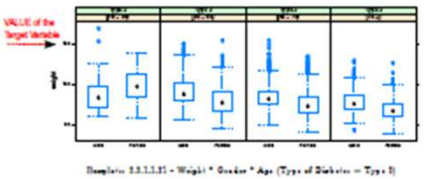
The density plot explores the distribution of target continuous variable: WEIGHT, WITHIN the Level of the Class Variable "Type of Diabetes"=2

Each section of the TRELLIS displays the distribution of the target variable (WEIGHT) for a particular combination of exposure factors (age, gender).

Lines can be used to compare the distribution of one exposure (gender) within the same level of the other exposure (age).

The continuous variable (WEIGHT) is automatically divided in a number of classes of equal range to display the frequency distribution. A curve is superimposed to show the shape of the density and explore the level of heterogeneity among exposure classes.

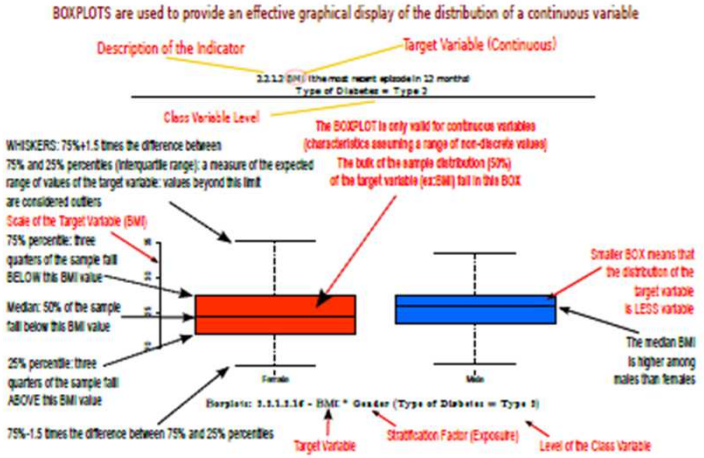
Here, the shape of the distribution of WEIGHT among young subjects shows a wider variation than higher ages, particularly for males. The distribution in older subjects is fairly normal.



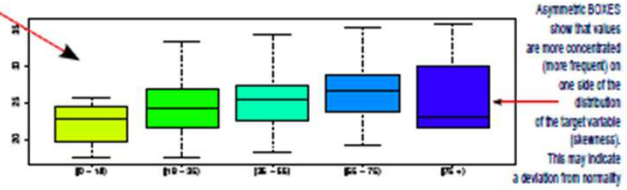
BOXPLOTS offer a synthetic view of the distribution of values (see BOXPLOT help for an explanation of the graph). Here, outlying values outside whiskers are highlighted by dots, showing a higher presence of extreme WEIGHT values in the central classes of age. The median value decreases with age. The median WEIGHT of males is constantly higher than females, except for younger subjects, for which holds the opposite.

HOW TO READ THE BIRO REPORT
BOXPLOTS

BOXPLOTS are used to provide an effective graphical display of the distribution of a continuous variable



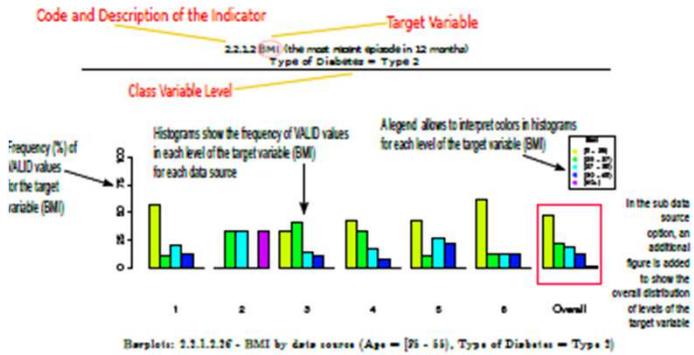
Stratification Factors with many levels (Age Classes) allow exploring direct associations between increasing levels of the exposure, and values of the target variable.
Here, with the exception of those aged 75+, BMI linearly increases with AGE. Whiskers show that also the variation of BMI is linearly increasing with AGE.



Boxplots: 2.2.1.2.17 - BMI * Age (Type of Diabetes = Type 2)

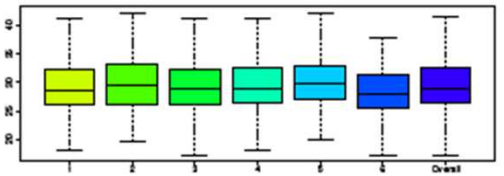
HOW TO READ THE BIRO REPORT
USING THE SUB DATA SOURCE OPTION

The SUB DATA SOURCE option can be used to compare the distribution of a target response across centres



Boxplots: 2.2.1.2.26 - BMI by data source (Age = [75 - 55), Type of Diabetes = Type 2)

In the SUB DATA SOURCE output, BOXPLOTS are used to compare distributions across centres for continuous response variables



Boxplots: 2.2.1.2.7 - BMI by data source (Type of Diabetes = Type 2)

Standardization

(AHRQ Quality Indicators)

Risk adjustment model (in each region)

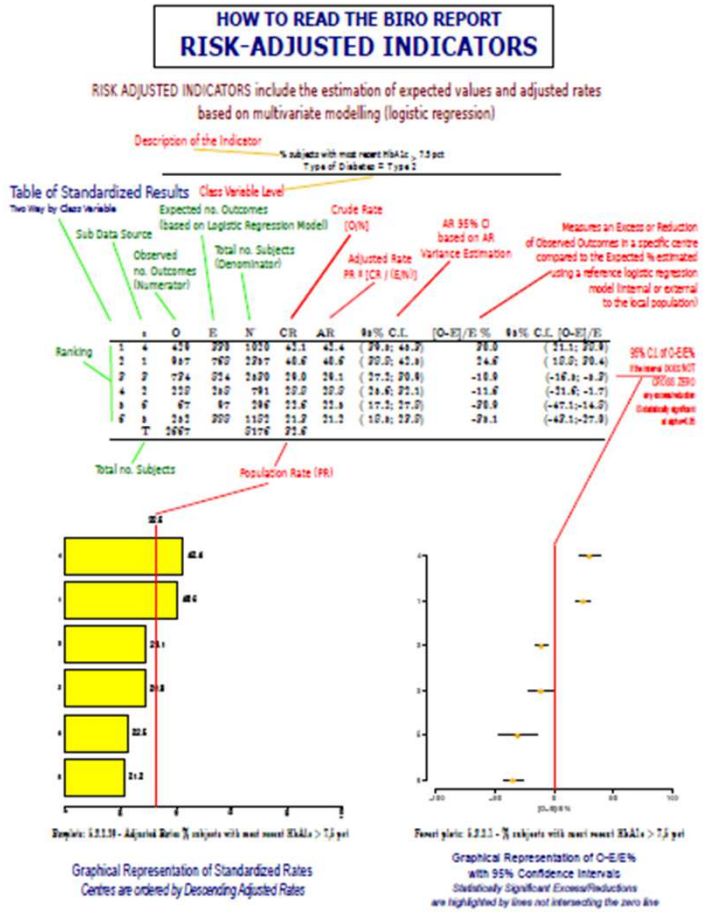
$$Y(\%) = \beta_0+\beta_1(\text{females})+\beta_2(\text{age\_class1})+...\beta_k(\text{age\_class4})$$

Source unit

Y_i expected= $\beta_0+\beta_1(\text{females})+\beta_2(\text{age\_class1})+...\beta_k(\text{age\_class4})$

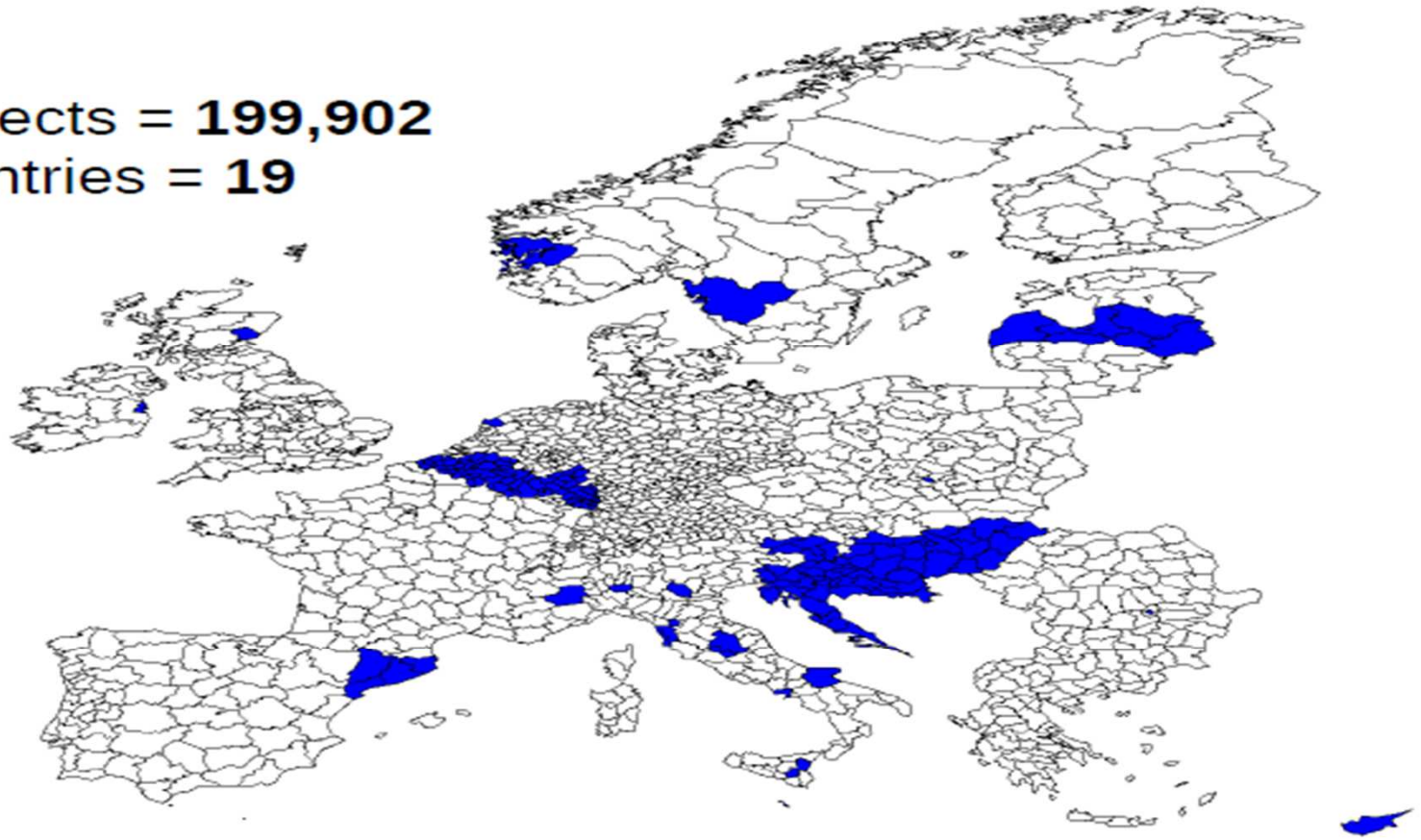
$\sum \text{Pred}_i \times 100 = \text{Expected Rate}$

Standardized Rate= (observed rate/expected rate)*population rate


HOW TO READ THE BIRO REPORT
RISK-ADJUSTED INDICATORS
RISK ADJUSTED INDICATORS include the estimation of expected values and adjusted rates based on multivariate modelling (logistic regression)
Description of the Indicator
Table of Standardized Results
Class Variable Level
Expected no. Outcomes (based on Logistic Regression Model)
Crude Rate (O/N)
Sub Data Source
Observed no. Outcomes (Numerator)
Total no. Subjects (Denominator)
Adjusted Rate PR # (CR / (E/N))
AR 95% CI based on AR Variance Estimation
Measures an Excess or Reduction of Observed Outcomes in a specific centre compared to the Expected % estimated using a reference logistic regression model (internal or external to the local population)
Ranking
95% CI of O-E/E%
Total no. Subjects
Population Rate (PR)
Graphical Representation of Standardized Rates
Centres are ordered by Descending Adjusted Rates
Graphical Representation of O-E/E%
with 95% Confidence Intervals
Statistically Significant Excess/Reductions
are highlighted by lines not intersecting the zero line

Geographical Coverage
EUBIROD Diabetes Report 2010

N Subjects = **199,902**
N Countries = **19**



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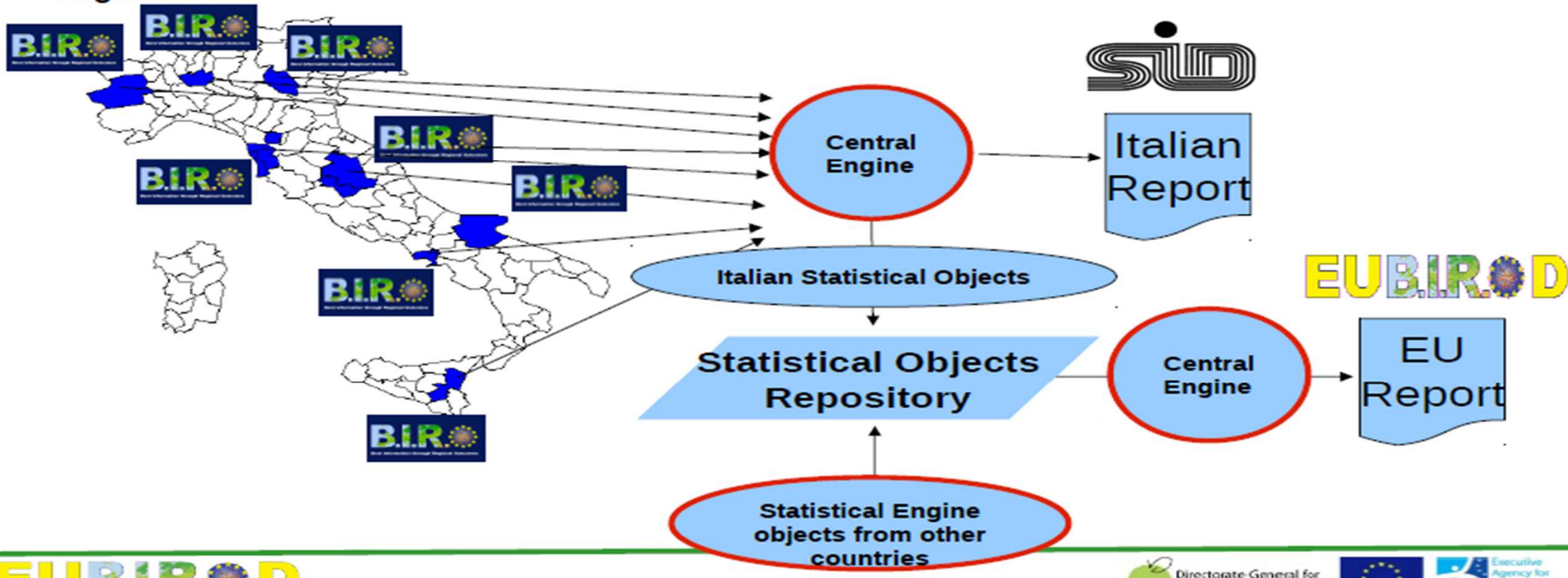
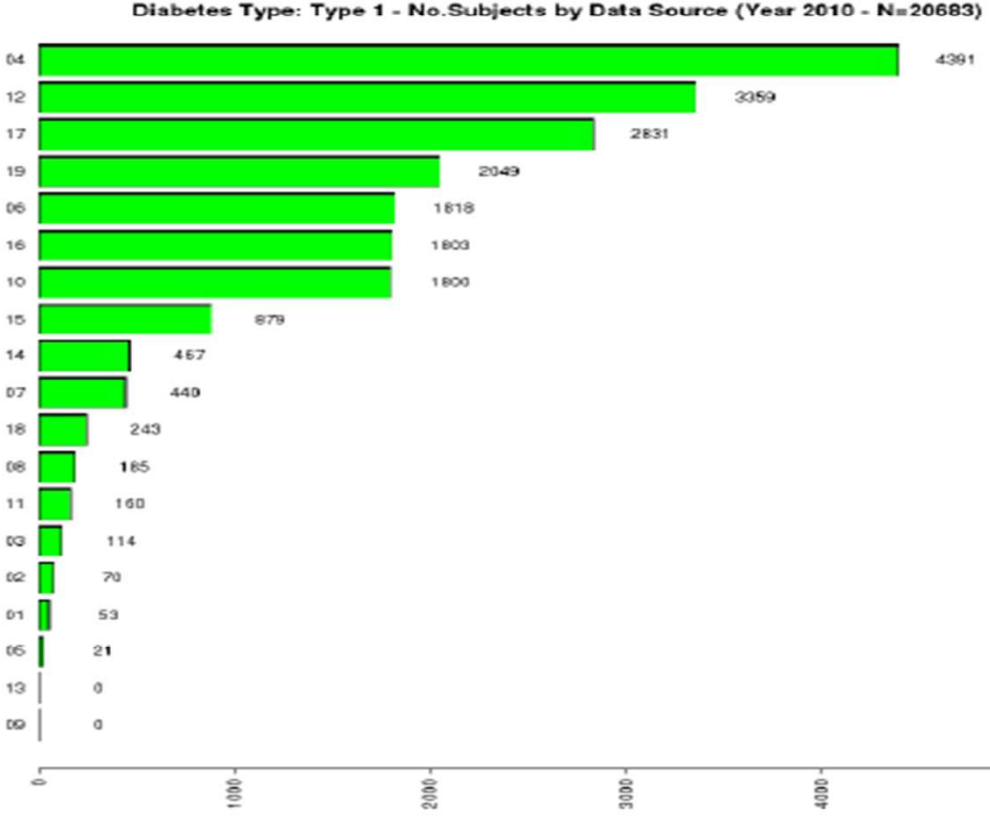
A crucial step

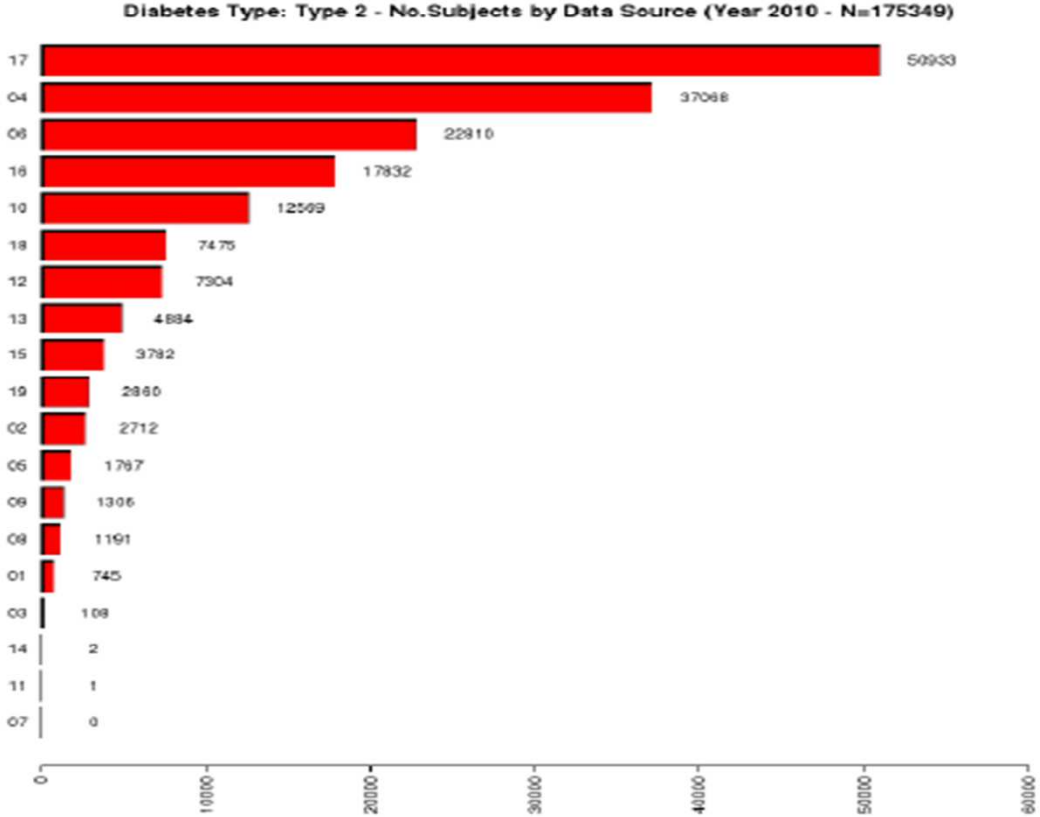
BIRO installed in N=7 clinical centres + Umbria Register (database split in N=6 sources). Data Import + Statistical Engine



TYPE 1-2

EUBIROD Diabetes Report 2010





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5.2.1 Percentage of Adults with 1+ HbA1c tests in 12 mts

Type 2 (N=172,605)

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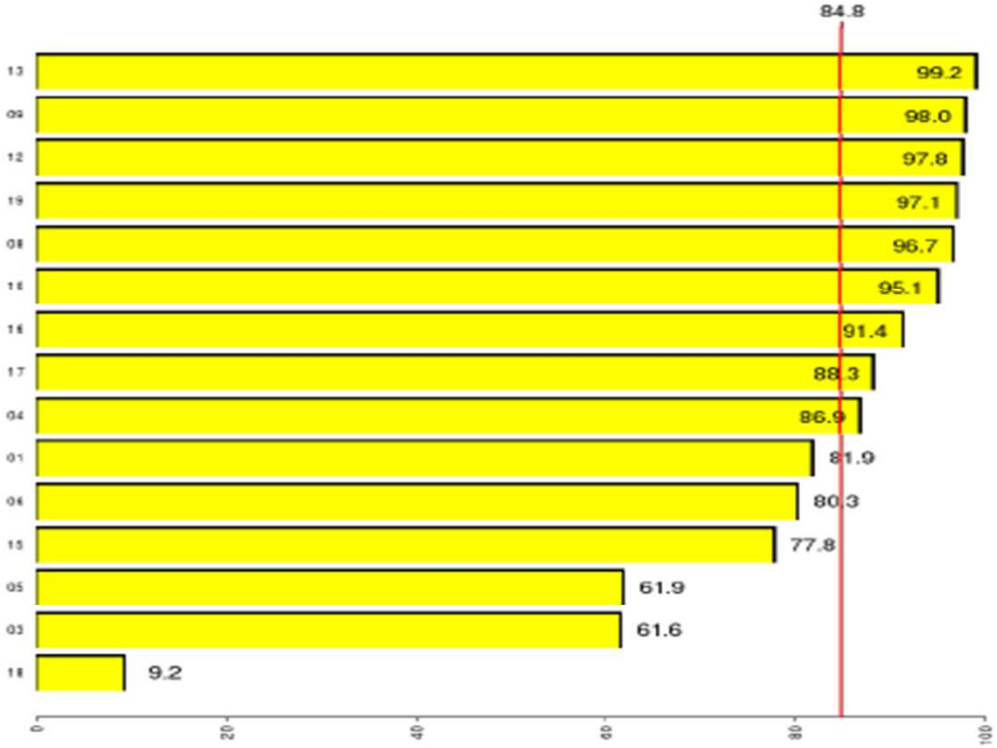

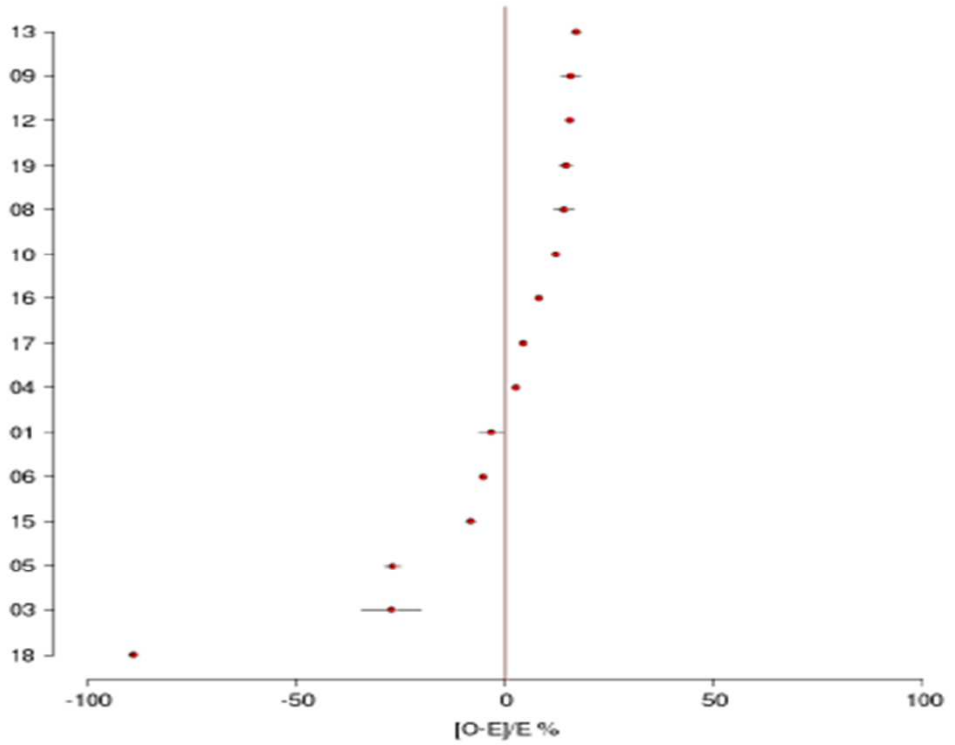

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5.3.1 Percentage of adults with most recent HbA1c>9.0%

Type 2 (N=146,397)

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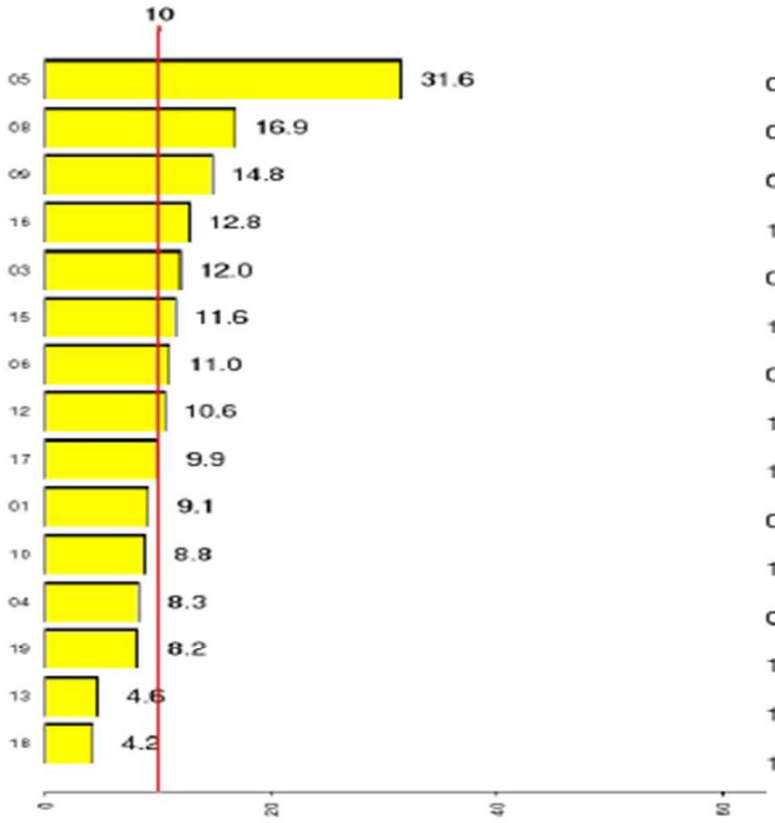

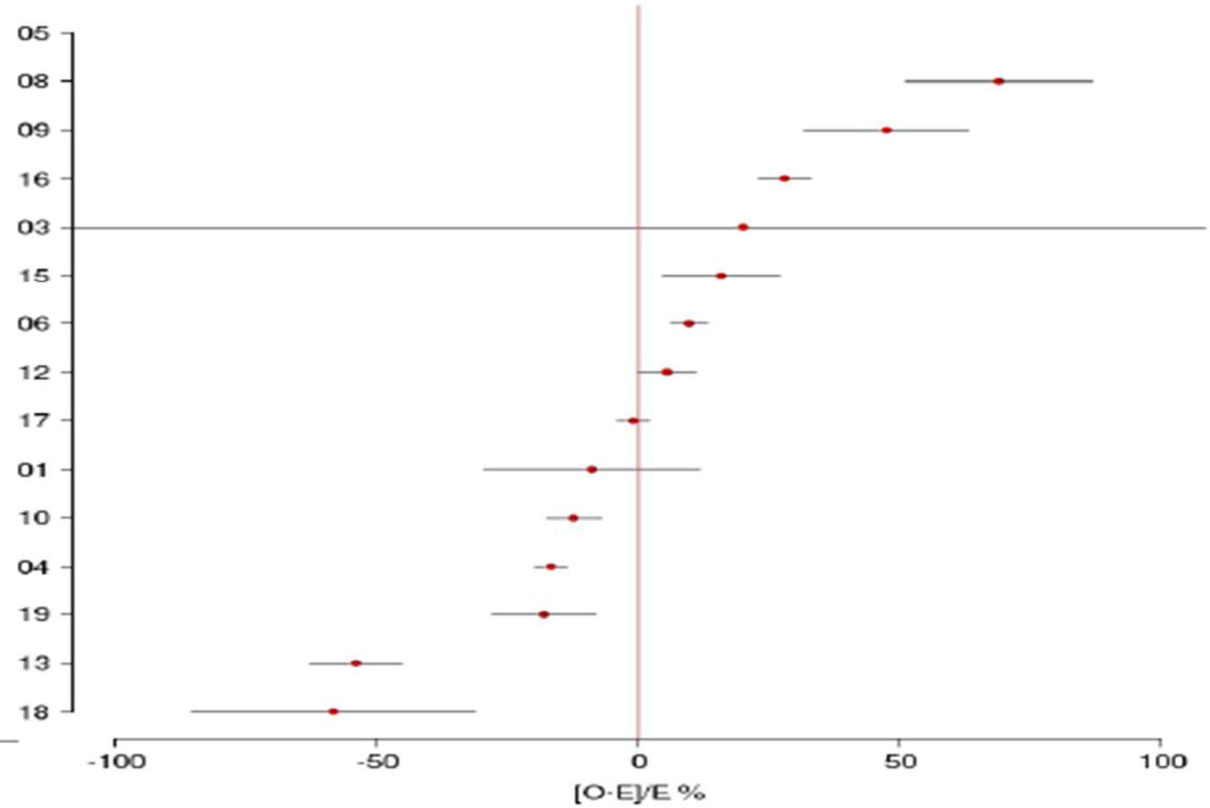

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2.2.3.6 HbA1c

N=168,948

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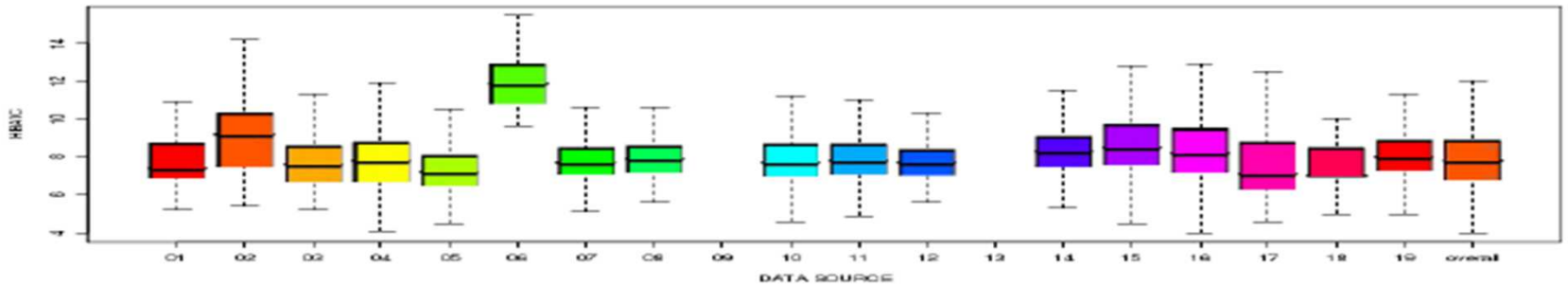
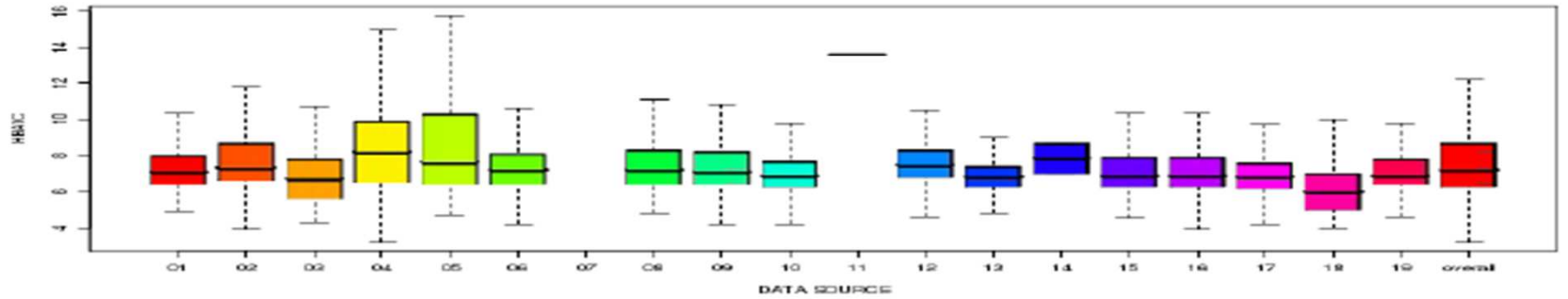
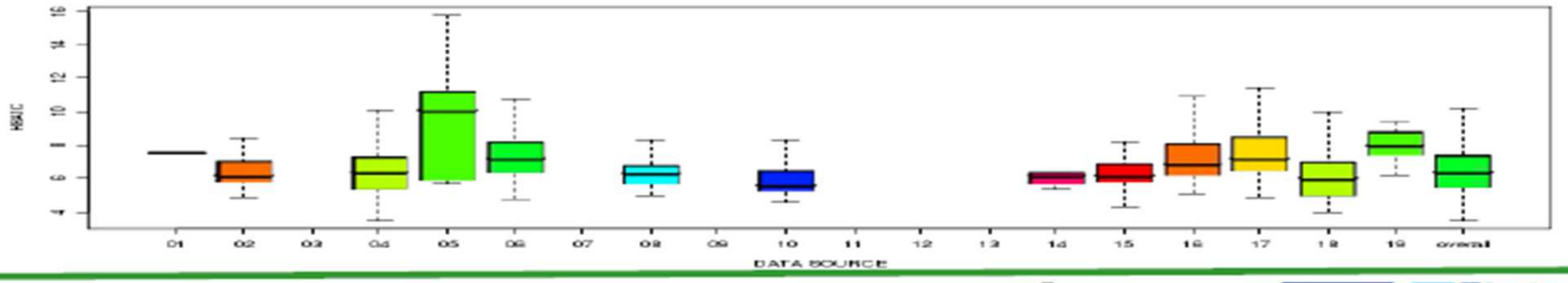
Type 1



Type 2



Other Type



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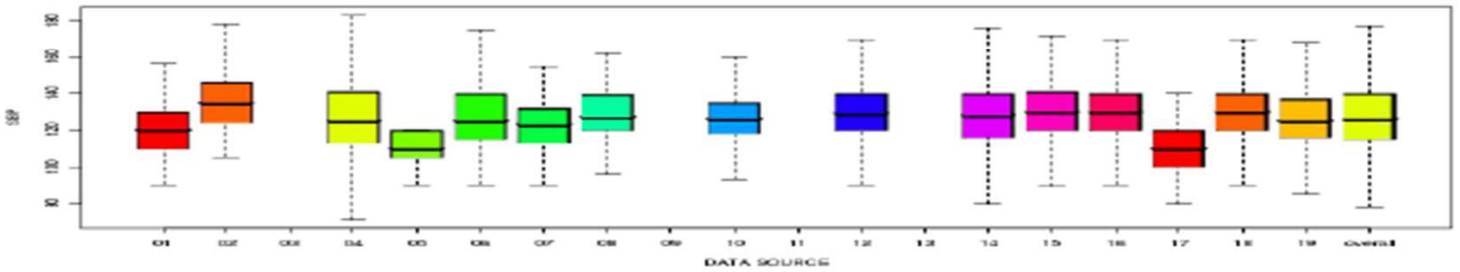
2.2.3.1. Systolic Blood Pressure

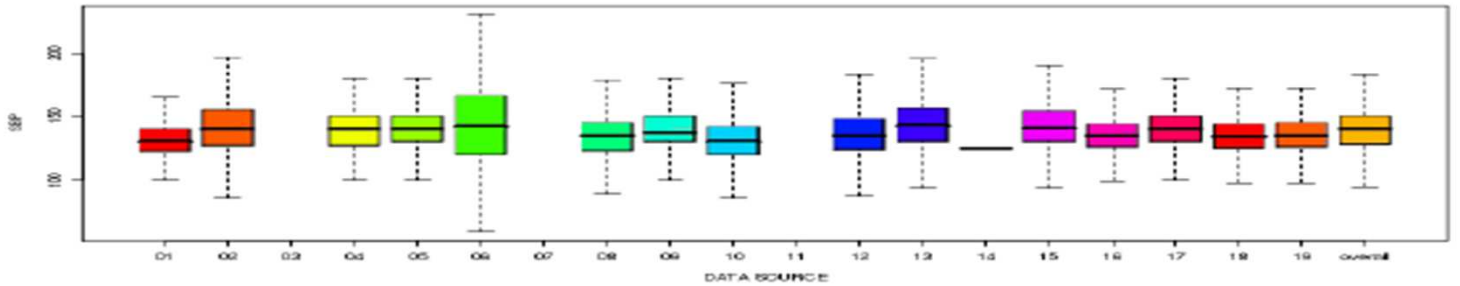
N= 170,046

EUBIROD Diabetes Report 2010

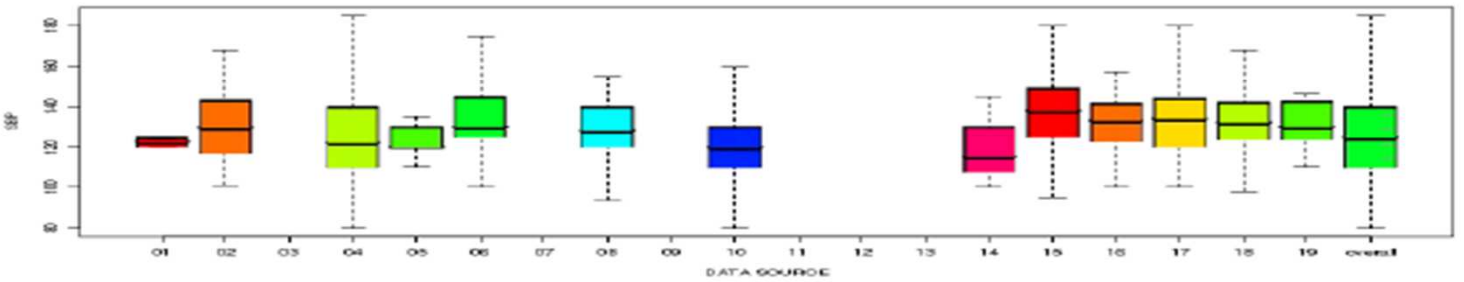
Type 1



Type 2



Other Type



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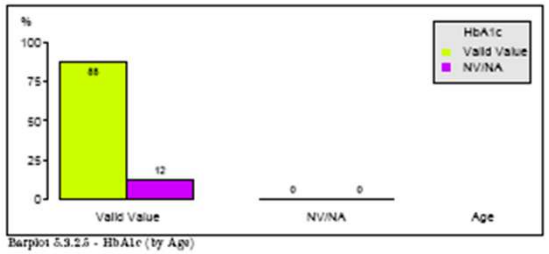
GLYCATED HbA1c GREATER THAN 7,5%

HbA1c	Valid Value (%)	NV/NA (%)	N (%)
Valid Value	95464 (88.0)	0(0.0)	95464 (88.0)
NV/NA	13055 (12.0)	0(0.0)	13055 (12.0)
TOTAL	108519(100.0)	0(0.0)	108519 (100.0)

Table 5.3.2.5 : HbA1c (by Age)

	CMH Chi-Square	p.value	df
Value	62581.1451	0	1

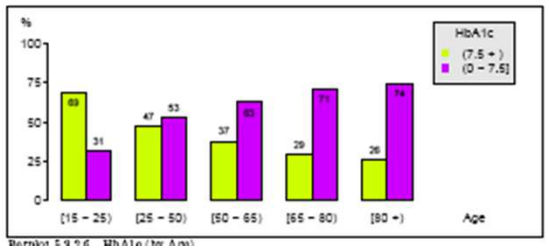


Barplot 5.3.2.5 - HbA1c (by Age)

HbA1c	[15 - 25) [%]	[25 - 50) [%]	[50 - 65) [%]	[65 - 80) [%]	[80 +) [%]	N [%]
(7.5 +)	927 [66.3]	8995 [47.2]	11938 [37.4]	11820 [29.4]	2883[25.9]	32979 [34.5]
[0 - 7.5]	471 [33.7]	6812 [52.8]	19994 [62.6]	27738 [70.6]	7671[74.1]	62485 [65.5]
TOTAL	1398[1.5]	12817[13.1]	31932[33.5]	39582[41.1]	10554[10.8]	95464 [100.0]

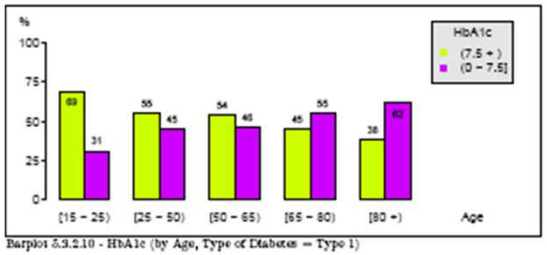
Table 5.3.2.6 : HbA1c (by Age)

	CMH Chi-Square	p.value	df
Value	2429.4346	0	4

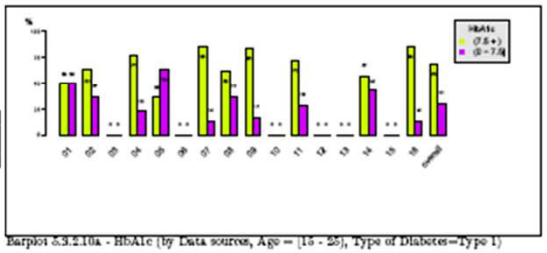


Barplot 5.3.2.6 - HbA1c (by Age)

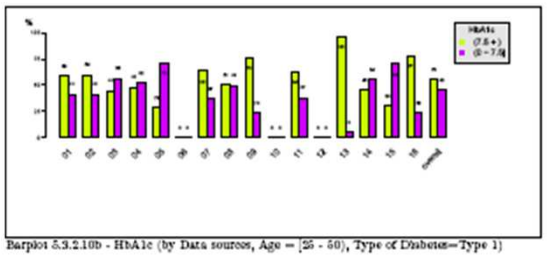
Type 1



Barplot 5.3.2.10 - HbA1c (by Age, Type of Diabetes = Type 1)

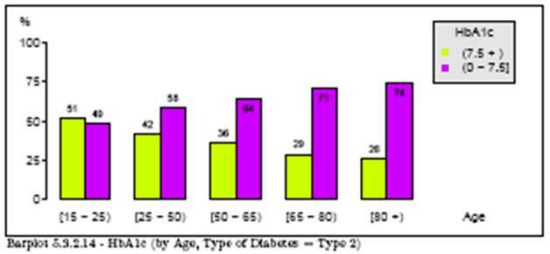


Barplot 5.3.2.10a - HbA1c (by Data source, Age = [15 - 25), Type of Diabetes=Type 1)

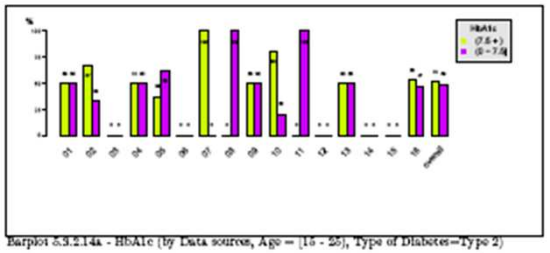


Barplot 5.3.2.10b - HbA1c (by Data source, Age = [25 - 50), Type of Diabetes=Type 1)

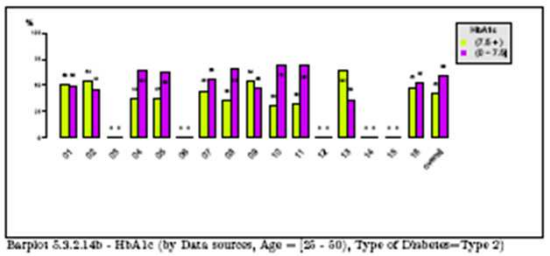
Type 2



Barplot 5.3.2.14 - HbA1c (by Age, Type of Diabetes = Type 2)



Barplot 5.3.2.14a - HbA1c (by Data source, Age = [15 - 25), Type of Diabetes=Type 2)



Barplot 5.3.2.14b - HbA1c (by Data source, Age = [25 - 50), Type of Diabetes=Type 2)

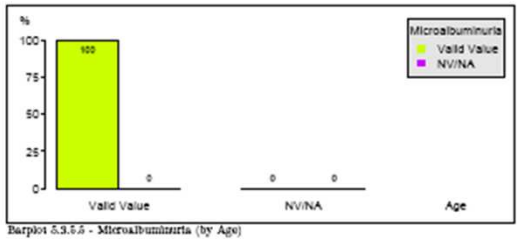
MICROALBUMINURIA

5.3.5 % of subjects with microalbuminuria in last 12 months (among those who have been tested)

Microalbuminuria	Valid Value (%)	NV/NA (%)		N (%)
Valid Value	44334 (100.0)	0(0.0)		44334 (100.0)
NV/NA	0 (0.0)	0(0.0)		0 (0.0)
TOTAL	44334(100.0)	0(0.0)		44334 (100.0)

Table 5.3.5.5 : Microalbuminuria (by Age)

CMH Chi-Square
Value Too many cells have 0 obs

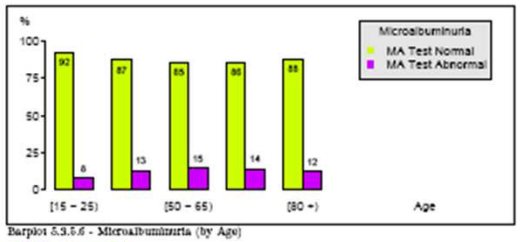


Barplot 5.3.5.5 - Microalbuminuria (by Age)

Microalbuminuria	[15 - 25) (%)	[25 - 50) (%)	[50 - 65) (%)	[65 - 80) (%)	[80 +) (%)	N (%)
MA Test Normal	611 (92.4)	5495 (87.1)	12559 (85.2)	15567 (85.9)	3995(87.9)	38217 (86.2)
MA Test Abnormal	50 (7.6)	811 (12.9)	2137 (14.5)	2567 (14.2)	553(12.1)	6117 (13.8)
TOTAL	661(1.5)	6306(14.2)	14696(33.1)	18134(40.9)	4547(10.3)	44334 (100.0)

Table 5.3.5.6 : Microalbuminuria (by Age)

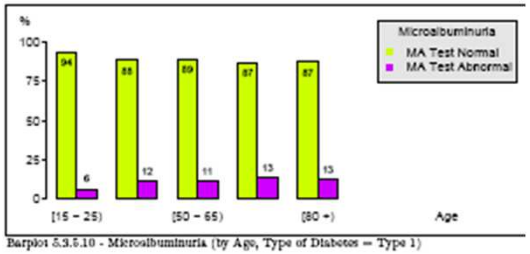
CMH Chi-Square	p.value	df
Value 45.3563	0	4



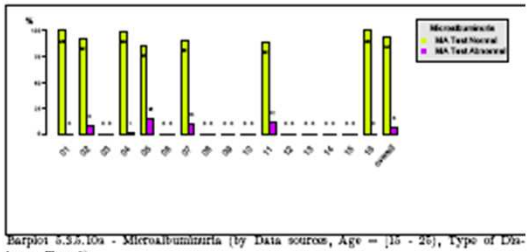
Barplot 5.3.5.6 - Microalbuminuria (by Age)

Type 1

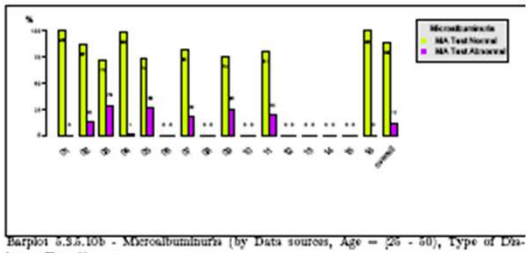
5.3.5 % of subjects with microalbuminuria in last 12 months (among those who have been tested)
Type of Diabetes = Type 1



Barplot 5.3.5.10 - Microalbuminuria (by Age, Type of Diabetes = Type 1)



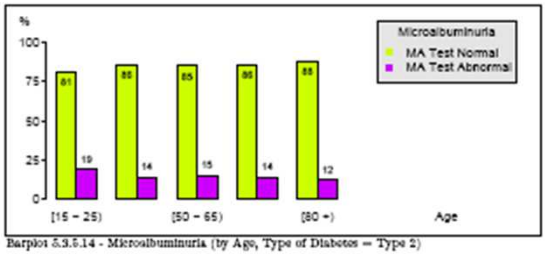
Barplot 5.3.5.10a - Microalbuminuria (by Data source, Age = [15 - 25), Type of Diabetes=Type 1)



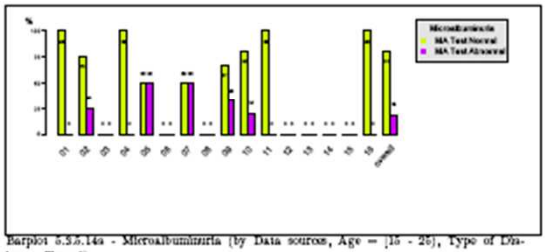
Barplot 5.3.5.10b - Microalbuminuria (by Data source, Age = [25 - 50), Type of Diabetes=Type 1)

Type 2

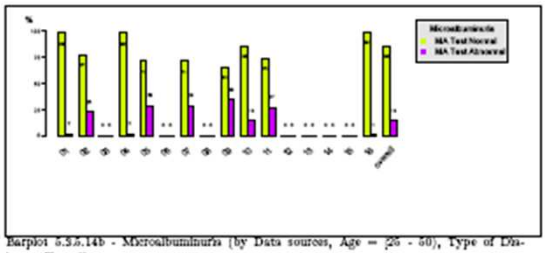
5.3.5 % of subjects with microalbuminuria in last 12 months (among those who have been tested)
Type of Diabetes = Type 2



Barplot 5.3.5.14 - Microalbuminuria (by Age, Type of Diabetes = Type 2)



Barplot 5.3.5.14a - Microalbuminuria (by Data source, Age = [15 - 25), Type of Diabetes=Type 2)



Barplot 5.3.5.14b - Microalbuminuria (by Data source, Age = [25 - 50), Type of Diabetes=Type 2)

EUBIROD

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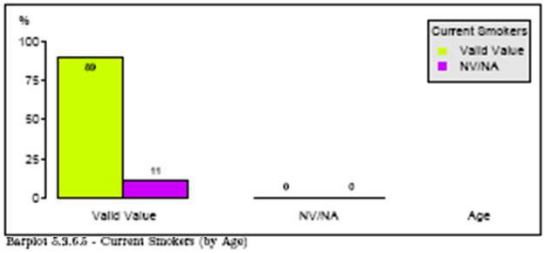
SMOKERS

Current Smokers	Valid Value (%)	NV/NA (%)	N (%)
Valid Value	88304 (89.5)	0(0.0)	88304 (89.5)
NV/NA	10360 (10.5)	0(0.0)	10360 (10.5)
TOTAL	98664(100.0)	0(0.0)	98664 (100.0)

Table 5.3.6.5 : Current Smokers (by Age)

	CMH Chi-Square	p.value	df
Value	61575.5176	0	1

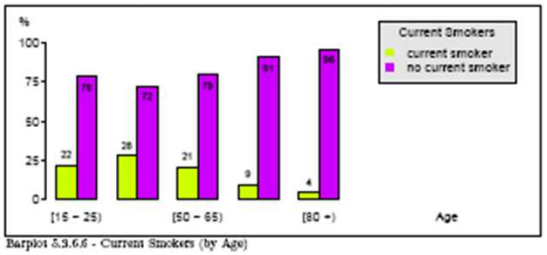


Barplot 5.3.6.5 - Current Smokers (by Age)

Current Smokers	[15 - 25) (%)	[25 - 50) (%)	[50 - 65) (%)	[65 - 80) (%)	[80 +) (%)	N (%)
current smoker	213 (21.7)	1271 (25.2)	6377 (20.6)	3404 (9.4)	409(4.4)	11674 (15.3)
no current smoker	767 (78.3)	6347 (71.5)	23965 (79.4)	32930 (90.6)	8880(95.6)	74759 (84.7)
TOTAL	980(1.1)	11618(13.2)	30342(34.0)	36334(41.1)	9289(10.5)	88233 (100.0)

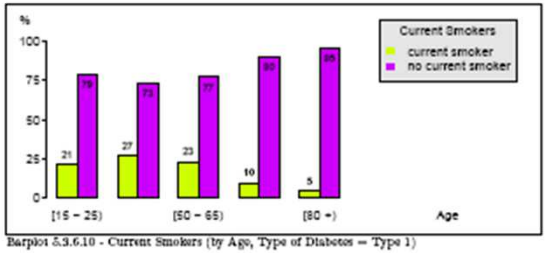
Table 5.3.6.6 : Current Smokers (by Age)

	CMH Chi-Square	p.value	df
Value	3994.7152	0	4

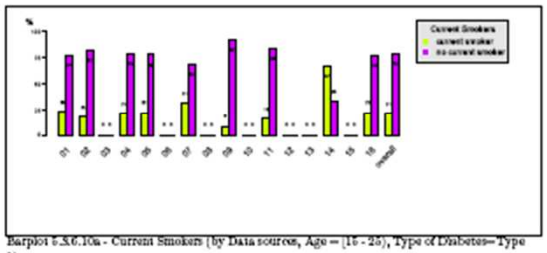


Barplot 5.3.6.6 - Current Smokers (by Age)

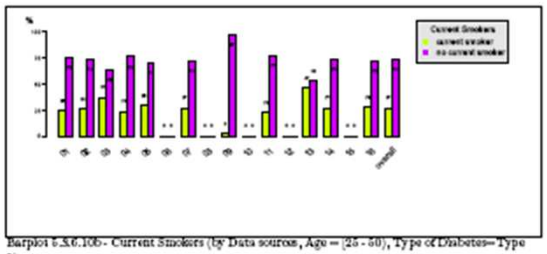
Type 1



Barplot 5.3.6.10 - Current Smokers (by Age, Type of Diabetes = Type 1)

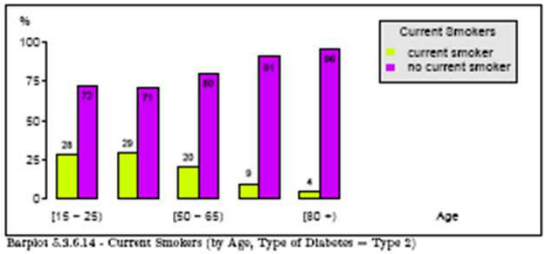


Barplot 5.3.6.10a - Current Smokers (by Data source, Age = [15 - 25), Type of Diabetes= Type 1)

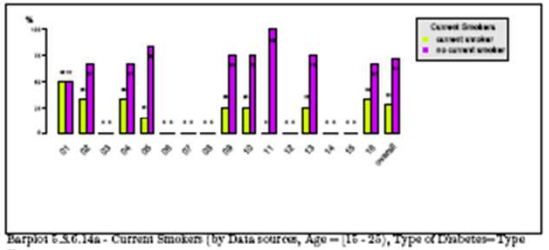


Barplot 5.3.6.10b - Current Smokers (by Data source, Age = [25 - 50), Type of Diabetes= Type 1)

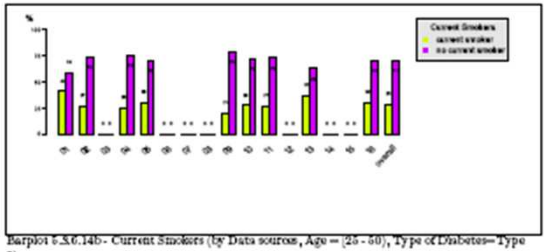
Type 2



Barplot 5.3.6.14 - Current Smokers (by Age, Type of Diabetes = Type 2)



Barplot 5.3.6.14a - Current Smokers (by Data source, Age = [15 - 25), Type of Diabetes= Type 2)



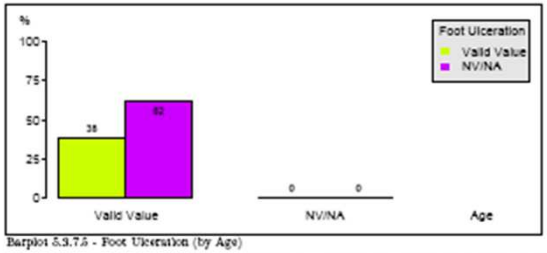
Barplot 5.3.6.14b - Current Smokers (by Data source, Age = [25 - 50), Type of Diabetes= Type 2)

Foot ulcers

Foot Ulceration	Valid Value (%)	NV/NA (%)		N (%)
Valid Value	33951 (38.0)	0(0.0)		33951 (38.0)
NV/NA	55343 (62.0)	0(0.0)		55343 (62.0)
TOTAL	89294(100.0)	0(0.0)		89294 (100.0)

Table 5.3.7.5 : Foot Ulceration (by Age)

	CMH Chi-Square	p.value	df
Value	5124.8429	0	1

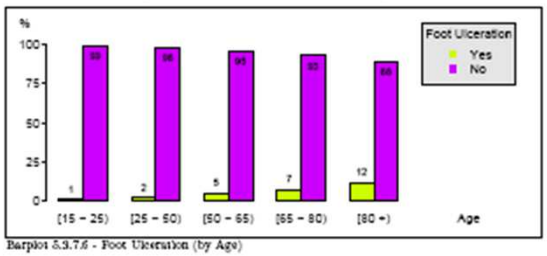


Barplot 5.3.7.5 - Foot Ulceration (by Age)

Foot Ulceration	[15 - 25) (%)	[25 - 50) (%)	[50 - 65) (%)	[65 - 80) (%)	[80 +) (%)	N (%)
Yes	5 (0.9)	115 (2.6)	504 (4.7)	1004 (7.2)	485(11.6)	2393 (6.2)
No	533 (99.1)	4644 (97.4)	10165 (95.3)	12991 (92.8)	3519(88.4)	31853 (93.8)
TOTAL	538(1.4)	4759(14.0)	10669(31.4)	13995(41.2)	3979(11.7)	33951 (100.0)

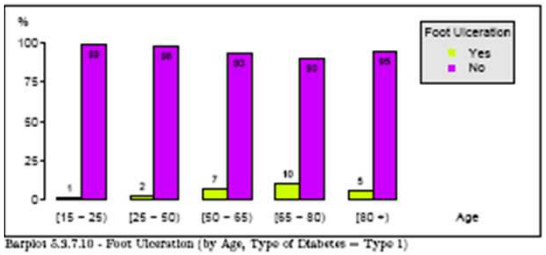
Table 5.3.7.6 : Foot Ulceration (by Age)

	CMH Chi-Square	p.value	df
Value	991.3107	0	4

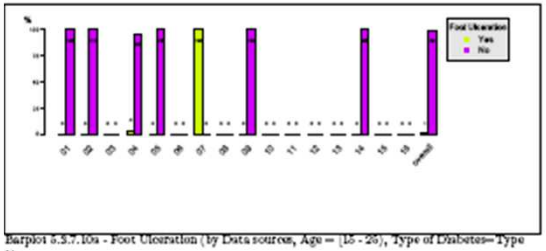


Barplot 5.3.7.6 - Foot Ulceration (by Age)

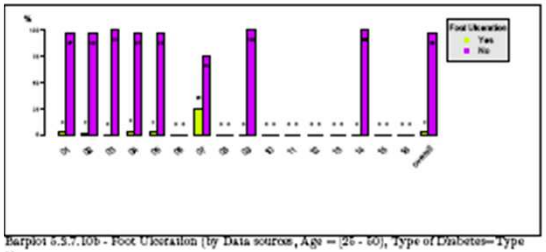
Type 1



Barplot 5.3.7.10 - Foot Ulceration (by Age, Type of Diabetes = Type 1)

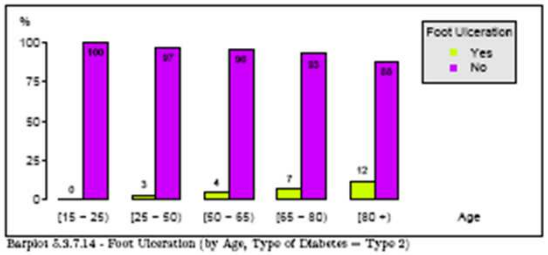


Barplot 5.3.7.10a - Foot Ulceration (by Data source, Age = [15 - 25), Type of Diabetes= Type 1)

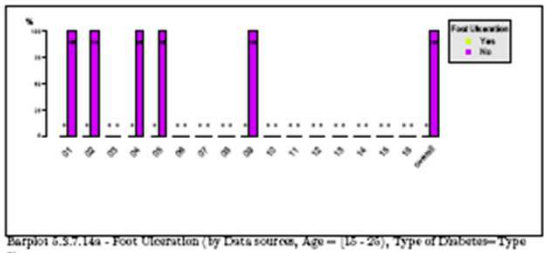


Barplot 5.3.7.10b - Foot Ulceration (by Data source, Age = [25 - 50), Type of Diabetes= Type 1)

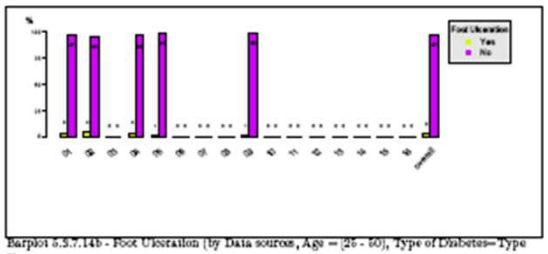
Type 2



Barplot 5.3.7.14 - Foot Ulceration (by Age, Type of Diabetes = Type 2)

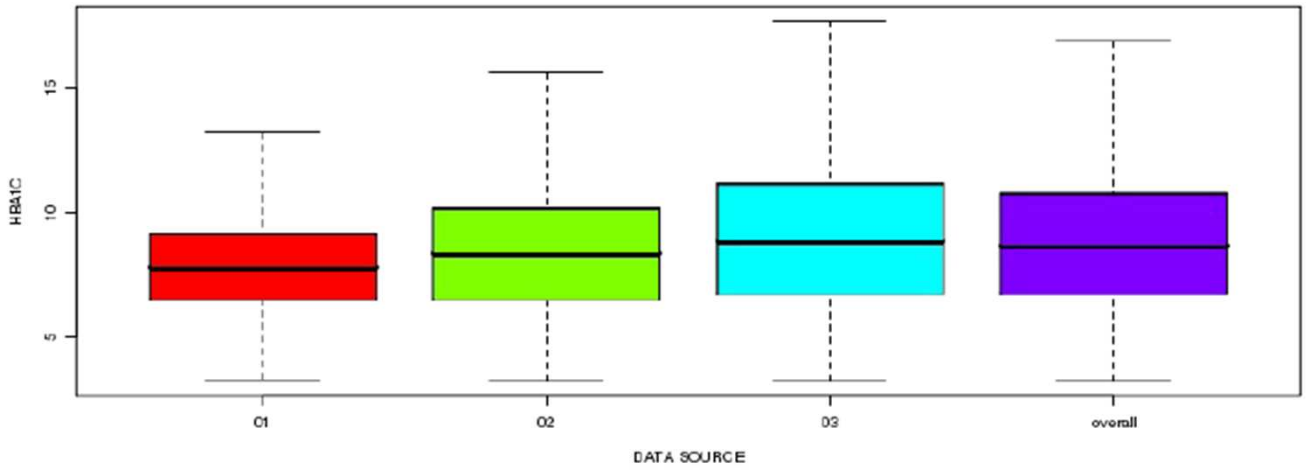


Barplot 5.3.7.14a - Foot Ulceration (by Data source, Age = [15 - 25), Type of Diabetes= Type 2)



Barplot 5.3.7.14b - Foot Ulceration (by Data source, Age = [25 - 50), Type of Diabetes= Type 2)

Recursive Central Engine on SO Repository
Example of Descriptive Results (1)



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Conclusions

EUBIROD has successfully realized the methodology for a European Diabetes Register through a coalition of multiple registers and different data sources

The BIRO technology is open, sustainable, generally valid and, most importantly, it has proved to work. The results can be now automatically linked to official EU platfoms in diabetes and across other chronic diseases

Our experience paves the way for a new generation of transnational/translational evidence-based information systems that can use distributed models with a higher efficiency and minimal impact on data privacy, ownership, and overall cost of information management

The implementation of distributed statistical systems e.g. BIRO may be initially complex, but once automated it can show all its advantages, particularly relevant for federal/decentralized health systems and large international partnerships

The plan of the BIRO project is motivated by the need to overcome some of the frequent barriers posed by problems like:

- insufficient utilization of information systems by clinicians and policy makers
- poor linkage between regional data sources and European statistical agencies
- limited application of sophisticated statistical routines in European health reports
- inadequacy of software available in the public domain
- insufficient use of medical records due to increasing privacy concerns
- lack of standardized approaches for secure data transmission

“Shared Evidence-based Diabetes Information System (SEDIS)”: an efficient and sustainable solution to perform the following tasks:

1. analysis of longitudinal trends and average outcomes in a diabetic population
2. identification of patterns of care and prevention consistently showing positive results
3. identification of population strata and/or practices that do not show effective results
4. verification of the application/applicability of best practice guidelines
5. on-field testing of collaborative information systems in chronic diseases