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Experimental and Real world data: collect, archive and share to increase their value in research

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Data sharing & Secondary use

Governments and funding agencies (*EC High Level Expert Group on Scientific Data 2010; National Institutes of Health 2016; National Science Foundation 2011; Organisation for Economic Co-operation and Development 2007*) promote the **sharing of scientific data** as a means **to make research products more widely available** for research, education, business, and other purposes (Pasquetto, I V et al 2017 On the Reuse of Scientific Data. Data Science Journal, 16: 8, pp. 1–9)

"**Health data constitutes a significant resource** in most OECD countries and it makes economic and ethical sense to use this data as much as possible **to improve population health and the effectiveness and the efficiency of health care systems**" (Secondary Analysis of Health Data to Generate Health Care Quality Information. Potential, Barriers and Best Practices in Data Linkage. Organisation for Economic Co-operation and Development, OECD DELSA/HEA/HCQ(2011)11)

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Data sharing & Secondary use

OPEN ACCESS TO RESEARCH DATA:

- Define clear policies for the dissemination of and open access to research data resulting from publicly funded research …
- … **research data that result from publicly funded research become publicly accessible, usable and re-usable** through digital e-infrastructures. Concerns in particular in relation to privacy, trade secrets, national security, legitimate commercial interests and to intellectual property rights shall be duly taken into account …
- datasets are made easily identifiable and can be linked to other datasets …

EUROPEAN COMMISSION

Brussels, 17.7.2012
C(2012) 4890 final

COMMISSION RECOMMENDATION

of 17.7.2012

on access to and preservation of scientific information

{SWD(2012) 221 final}
{SWD(2012) 222 final}

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Data sharing & Secondary use

The **National Institutes of Health** require that **federally funded studies** receiving over $500,000 per year have a **data sharing plan** describing:

- how data will be shared
- how shared data will be made available in a usable form
- for which extended period of time

It is also required that **the least restrictive method** for sharing of research data should be used, provided it maintains scientific **integrity** and appropriate **protection** for participants (Plan for Increasing Access to Scientific Publications and Digital Scientific Data from NIH Funded Scientific Research, Feb. 2105; Acquiring and Using Electronic Health Record Data | Rethinking Clinical Trials® https://sites.duke.edu)

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Data sharing & Secondary use

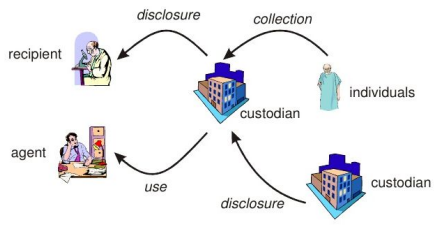
To achieve the expected benefits of data sharing, data must actually be **reused** by others

Secondary use of data occurs when data is used for a purpose different from the purpose for which the data was initially collected

(Bahr A et Al. Code of practice on secondary use of medical data in European scientific research projects. International Data Privacy Law, Volume 5, Issue 4, 1 November 2015, Pages 279–291)

Secondary use of data is defined as "non-direct care use of personal health information including but not limited to analysis, research, quality/safety measurement, public health, payment, provider certification or accreditation, and marketing and other business including strictly commercial activities"

(Safran et al. "Toward a National Framework for the Secondary Use of Health Data: An American Medical Informatics Association White Paper," JAMIA 2007 14, 2, fn 1)



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Data sharing & Secondary use

- Gaining permission to use the data
- Assessing the availability of data for a research need
- Assessing the quality of the data
- Identifying the needed data for the population of interest
- Linking data from different sources
- Managing the data for the duration of a given study

- Source systems (bed-side monitor, local labs, central lab, imaging, ...)
- Clinical work flow uniformity and changes over time of the way data are being collected
- Consistency
- Completeness
- Row data value

MAIN ISSUES

- Data sharing rules and regulations, data privacy and security issues
- **Data standards (compatibility)**
- Local diversities (tools, languages, organization, …)
- Healthcare practices and regulations
- Interoperability of systems
- Adequacy and consistency of clinical documentation

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Secondary use of health data:

- may deal with analysis, research, quality and safety measurement, public health, payment, provider certification or accreditation, marketing, and other business applications, including strictly commercial activities
- can enhance health care experiences for individuals, expand knowledge about disease and appropriate treatments, strengthen understanding about effectiveness and efficiency of health care systems, support public health and security goals, and aid businesses in meeting customers' needs

Complex ethical, political, technical, and social issues are raised by the secondary use of health data

Need for a robust infrastructure of policies, standards, and best practices to get the most from secondary use of data

(Safran et al. "Toward a National Framework for the Secondary Use of Health Data: An American Medical Informatics Association White Paper," JAMIA 2007 14, 2, fn 1)

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Data sharing & Secondary use

EU General Data Protection Regulation facilitates **better use** of personal data

General Data Protection Regulation (GDPR) EU 2016/679 **25 May 2018**

The new Regulation will also guarantee **free and easy access to your personal data**, making it **easier** for you to see what personal information is held about you by companies and public authorities, and make it easier for you to **transfer your personal data** between service providers – the so-called principle of 'data portability'.

Privacy means that **personal data** should not be secured from being used, but **to be used securely**

DIGITAL FUTURE HEALTH and CARE, Madrid Sept. 2017: *Ain Aaviksoo. Deputy Secretary General for E-services and Innovation, Ministry of Social Affairs of the Republic of Estonia*

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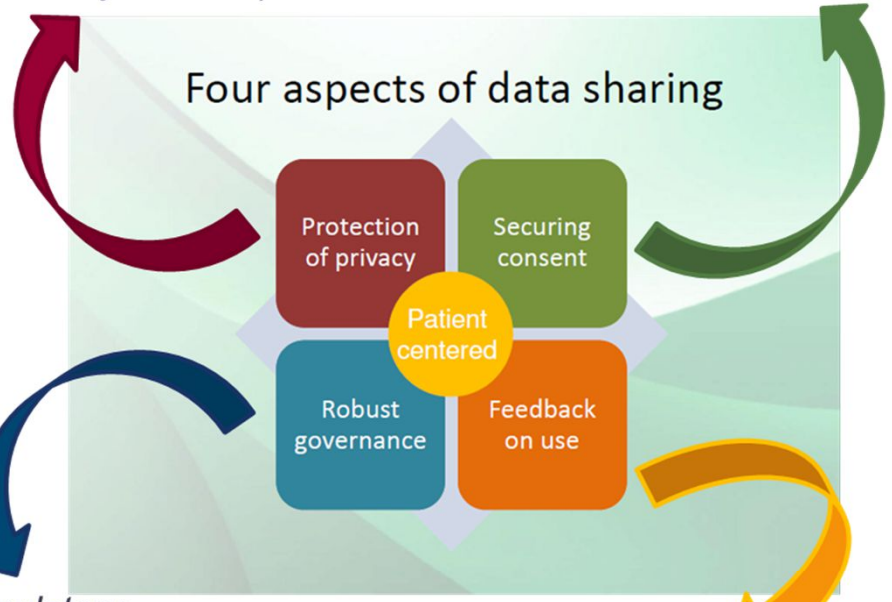
Data sharing & Secondary use

*Risk should be mediated trough **safeguards** (including data minimization, anonymisation and pseudo-anonymization)*

Consent has to be given by a clear affirmative action establishing a freely given, specific, and unambiguous indication of agreement to data processing



PATIENTS NEED & EXPERIENCES.
Simona Bellagambi. EUORDIS. 4° International Summer School on Rare Diseases and Orphan Drug Registries. ISS. Rome, 2016

A common regulatory framework should facilitate data sharing and harmonise protection of sensitive data and include patients

Outcomes of data-sharing activities should be communicated. Personal patient data can be reused for other purposes provided that his/her rights are ensured:
- *Patient must be informed on other purposes,*
- *must express new consent if previous for different purposes,*
- *have the right to object to the new purpose*

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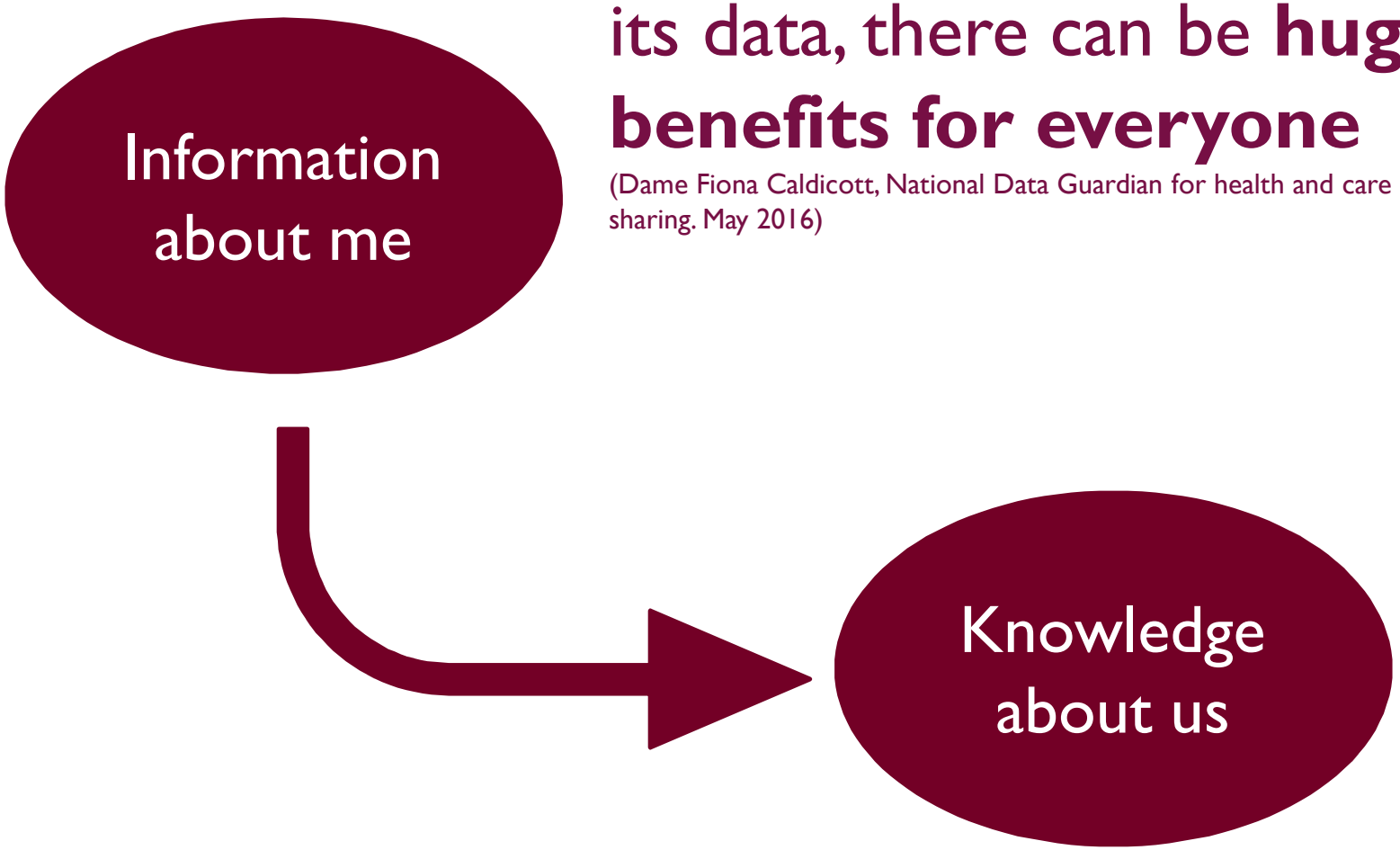
Data sharing & Secondary use

If the public is willing to trust health and care services with its data, there can be **huge benefits for everyone**

(Dame Fiona Caldicott, National Data Guardian for health and care on data-sharing. May 2016)



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Data Sharing methods

1 - **Open access**

Data is prospectively posted on to a public website. Individual researchers can access these data without having to go through a formal research request review process and they are able to download datasets and hold copies on their own computers.

2 - **Direct Sharing**

Following approval of a data sharing request, the data holder provides copies of de-identified data directly to the researcher. (using secure file transfer protocol (SFTP) or other secure electronic transfer system, and assuring the compliance with data security of recipient's IT system

3 - **Controlled access**

Following review and agreement of the research proposal by a review panel, the researcher is given access to the secure website and they perform all their programming and analysis within the system. The researcher is able to download analysis results but is not able to download the datasets. There may be the facility for the researcher to upload data and programs into the secure website. Again, a data sharing agreement may be set up between the researcher and the Data Holder.

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Data Sharing methods
Open Access

"Publicly funded research data are a public good, produced in the public interest, which should be made openly available with as few restrictions as possible in a timely and responsible manner"

Organisation for Economic Co-operation and Development, European Commission, National Institutes of Health, and the G8 science ministers

National Institute for Drug Abuse (NIDA) Clinical Trials Network (CTN)
www.ctndatashare.org

Documents provided:

- the study protocol
- reference to study publication of primary outcome
- data sets (SAS and ASCII)
- annotated data collection forms
- data dictionary defining each data element
- study-specific de-identification notes

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Data Sharing methods
Direct Sharing

Aims to develop procedures to provide the scientific community with access, upon request, to the individual participant data (IPD) from previous clinical trials for re-analyses, secondary analyses and meta-analyses.

Yale University Open Data Access (YODA) http://yoda.yale.edu/

Requests considered and evaluated on an individual basis.

Different possibilities, according to the Data Holder. Examples:

- data available (not downloadable or copied) through a password-protected personalized account on a secure data sharing platform.
- transfer of data directly to the requestor via a secure electronic data transfer system. Data may need to be downloaded in order to be used.

Data Use Agreement to be signed

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Data Sharing methods
Controlled Access

EMA - Data sharing methods

"The User acknowledges that the Clinical Reports will be made available to the User on the EMA website in a "view-on-screen-only" mode, after completing the registration process. The User agrees that the User is not permitted to download, save, edit, photograph, print, distribute or transfer the Clinical Reports. The User agrees not to access the Clinical Reports using a method other than the interface provided by the EMA, or remove, bypass, circumvent, neutralise or modify any technological protection measures which apply to the Clinical Reports."

Phase 1

Publication of clinical reports submitted to the Agency, regardless of the outcome of the regulatory procedure (entered into force on 1 January 2015)

Phase 2

Publication individual patient data (IPD). EMA will implement this phase at a later stage.

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Data Sharing methods

	EMA - Clinical data	NIDA Data Share Website - National Institute on Drug Abuse	eyeGENE® (National Ophthalmic Disease Genotyping and Phenotyping Network)	YODA project (Yale University Open Data Access)	Clinical Study Data Request (CSDR)
Registration	Two levels (View and Download)	the user is prompted to complete a registration agreement for data use only providing a name and valid e-mail address	Yes	Yes	Yes
Data Sharing Agreement	No	Users during the registration accept their responsibility for using data in accordance with the NIDA Data Share Agreement	Yes	Yes	Yes
Requirements to access data	Only Academic user accounts can access and download clinical reports; a specific registration is required	Only registration	All researchers interested in accessing clinical data, genetic analysis data, and DNA samples from eyeGENE® must submit a proposal for approval from the Resource Access Subcommittee (eGRASC).	Submission of a project proposal to be accepted	Registered researchers can submit research proposals and request anonymised data from clinical studies listed on this site. It is also possible to request or access study documents without patient-level data.
Secure Safe Harbor platform	No	No	No	Yes	Yes
Download data/information	Yes	Yes	Yes	Yes	Only the analysis performed on the Secure Safe Harbor platform

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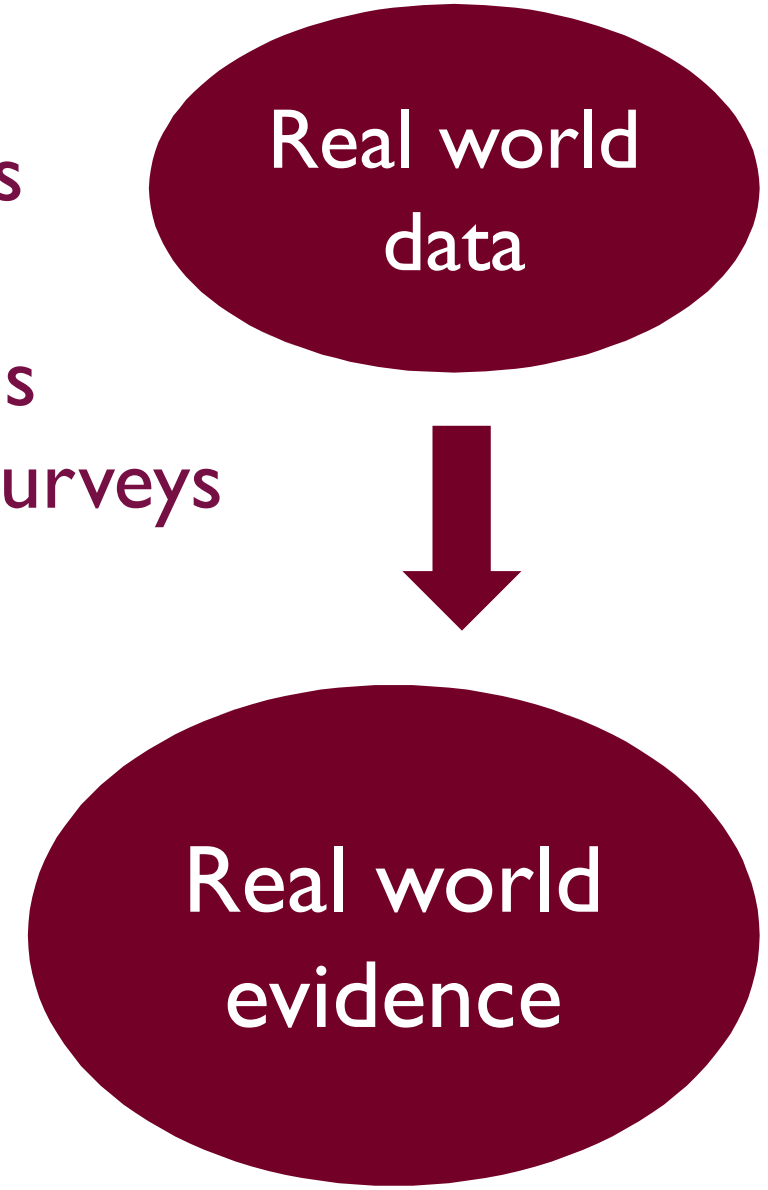
Sources of health data

- Public registries
- Administrative databases
- Clinical records
- Electronic health records
- Population and patient surveys
- GPs databases
- Pragmatic trials
- **Patient registries**
- …



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Patient registries

PATIENT REGISTRIES are organised systems that use observational methods to collect uniform data on a population defined by a particular disease, condition, or exposure, and that is followed over time.

Patient registries can play an important role in monitoring the safety of medicines.

The EMA has set up an initiative to make better use of existing registries and facilitate the establishment of high-quality new registries if none provide adequate source of post-authorisation data for regulatory decision-making

[Initiative for Patient Registries, 2015]
(www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000658.jsp)

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Patient registries

Properly designed and executed, **PATIENT REGISTRIES** can provide a real-world view of clinical practice, patient outcomes, safety, and comparative effectiveness:

- to observe the course of disease;
- to understand variations in treatment and outcomes;
- to examine factors that influence prognosis and quality of life;
- to describe care patterns, including appropriateness of care and disparities in the delivery of care;
- to assess effectiveness;
- to monitor safety and harm;
- to measure quality of care;
- to study quality improvement.

[Registries for Evaluating Patient Outcomes: A User's Guide. 3rd edition. AHRQ Agency for Healthcare Research and Quality]

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Patient registries

Registries can be used to:

- ✓ Evaluating patient outcomes including patient reported outcome measures (PROMs)
- ✓ Providing cost effectiveness data
- ✓ Providing safety information e.g. side effects and adverse events
- ✓ Providing data on the natural history of a disease or outcomes using current best available treatment
- ✓ Facilitating the recruitment of an adequate sample size
- ✓ Facilitating the use of case control methodologies
- ✓ Providing the infrastructure for post licencing studies
- ✓ Assessing the dissemination of outcomes from the HTA process

[Patient registries in Ireland]

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Value of Patient Registries

- Better understanding of the natural history of the disease
- To develop sensitive Disease Severity Index
- To identify Genotype/phenotype correlations
- To collect natural history data can be used to develop and refine disease specific QoL questionnaires to collect patient perspective
- To evaluat patient outcomes including patient reported outcome measures (PROMs)
- To provid cost effectiveness data
- To provid safety information e.g. side effects and adverse events
- To provid the infrastructure for post licencing studies
- Collaboration research teams and patient organization and industry to help identify end points as well as effective patient recruitment for clinical trials
- To set the scene for collecting long-term real world data, as required by regulators and policymakers
- To assess the dissemination of outcomes from the HTA process

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Patients Registries

"Key tools to increase knowledge on rare diseases and facilitate research in the field of rare diseases"

(Commission Communication 2009/C 151/02):

Patient registries:

- collect homogeneous data
- evaluate specific outcomes
- respond to specific clinical questions
- respond to organizational needs or health policy

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Use of Patient Registries

Thalassemia Reports 2014; volume 4:4875

pagepress

Comorbidities at baseline

Multidisciplinary care in haemoglob

Adriana Ceci,[1,2] Laura Mangiarini,[1] Fedele E
HTA-THAL Multiregional Registry

[1]Consorzio per Valutazioni Biologiche e Farma

Table 3. Cost of the care and hepatitis C.

	With hepatitis						P
Transfusion serv							
ICT							
Additional visit /							
Additional Drug							
New clinical eve							
Total							

Table 4. Instrumental Iron Overl

Iron monitoring	< 6 yr (N=51						P
Hepatic MRI	7 (13.7%						<0.001
Hepatic SQUID	6 (11.8%)	20 (25.0%)	15 (12.1%)	15 (5.8%)	33 (4.3%)	5 (4.0%)	112 (6%)	<0.001
Cardiac MRI	6 (11.8%)	25 (31.3%)	56 (52.3%)	137 (60.9%)	756 (58.5%)	55 (50.9%)	1035 (55.9%)	<0.001
Hepatic and cardiac MRI	6 (11.8%)	18 (22.5%)	49 (45.8%)	128 (56.9%)	716 (55.9%)	53 (49.1%)	970 (52.4%)	<0.001

Table 5. Patients' satisfaction with services.

Patient Satisfaction	Yes	No
Comprehensive approach at centres level	27%	73%
Services integration at local level		
Nursing	40%	60%
Medical	18%	82%
Social	42%	58%
Patients associations integration	40%	20%
New therapies informations	34%	26%
Research funds	25%	35%

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Use of Patient Registries

New Complications Pattern and burden of the disease in patients affected by beta-thalassemia major

F. Bonifazi, R. Conte, P. Baiardi, D. Bonifazi, M. Felisi, P. Giordano, V. Giannuzzi, A. Iacono, R. Padula, A. Pepe, MC Putti, L. Ruggieri, G.C. Del Vecchio, A. Filosa, A. Maggio, A. Ceci, on behalf of the HTA-THAL Multiregional Registry (*under final revision*)

… the presence of cardiovascular diseases was lower than expected

… very high frequency of the observed osteoporosis and

A relevant complications' group is represented by ipogonadism

We have observed a relatively high number of thrombotic complications that are considered more common in thalassemia intermedia than in regularly transfused thalassemia major (Panigrahi I, 2007) thus the number observed in our series should be considered and discussed

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Use of Patient Registries

Taylor & Francis

Hematology

ISSN: 1024-5332 (Print) 1607-8454 (Online) Journal homepage: http://www.tandfonline.com/loi/yhem20

The Italian Multiregional Thalassemia Registry: centers characteristics, services and patients' population

R. Conte, L. Ruggieri, A. Gambino, F. Bartoloni, P. Baiardi, D. Bonifazi, F. Bonifazi, M. Felisi, V. Giannuzzi, R. Padula, A. Pepe, M.C. Putti, G.C. Del Vecchio, A. Maggio, A. Filosa, A. Iacono, L. Mangiarini & A. Ceci

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To link to this article: http://dx.doi.org/10.1080/10245332.2015.1101971

Concluding, this analysis confirms the utility of PATIENT REGISTRIES for the collection of large set of data. In particular, the considerations derived from this data set highlight how the use of large, well-monitored PATIENT REGISTRIES can guide Health Authorities and Health providers to plan cost-effective services and to meet patients' needs and expectations.