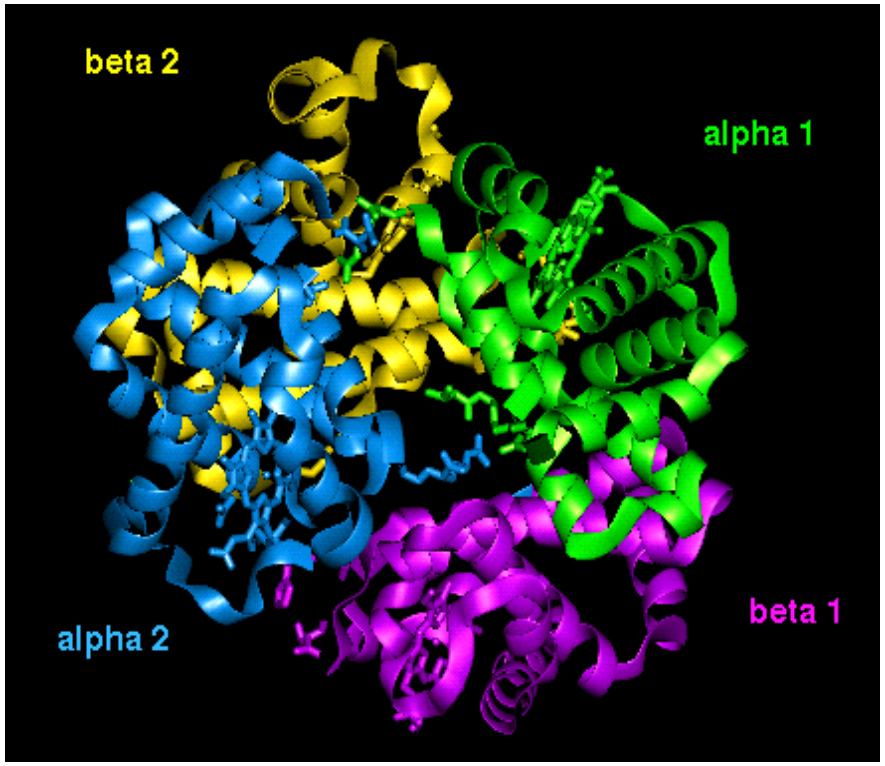
SITE
SOCIETA' ITALIANA
TALASSEMIE ED EMOGLOBINOPATIE

Gian Luca Forni

Presidente della «Società Italiana Talassemie ed Emoglobinopatie» (SITE)

6 Luglio 2021



Emoglobina: proteina deputata a veicolare l'Ossigeno nell'organismo

EMOGLOBINOPATIA

Alterazione ematologica, talvolta associata ad anemia, dovuta ad un difetto congenito di una o più globine, costituenti il tetramero dell’emoglobina

Circa il 7% della popolazione mondiale è portatore di anomalie ereditarie dell'emoglobina, rendendole in assoluto le più comuni malattie monogeniche

Circa il 10% della popolazione Italiana è portatrice asintomatica di una anomalia della Emoglobina

Annals of Human Biology, March–April 2005; 32(2): 117–122

The global problem of genetic disease

Sickle cell disease as a paradigm of immigration hematology: new challenges for hematologists in Europe

Irene Roberts, Mariane de Montalembert

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D. J. WEATHERALL

Weatherall Institute of Molecular Medicine, University of Oxford, UK

Abstract

Inherited haemoglobin disorders will undoubtedly cause an increasing health burden in many developing countries. Although much is known about their molecular pathology and the mechanisms for their phenotypic diversity, many important questions remain, not least the role of the environment in modifying the clinical course. Methods for screening these conditions are now well established and inexpensive and it is vital that they are applied to define the magnitude of the problem that will be posed by these conditions in the future. Similarly, they form the basis for widespread screening and counselling programmes directed at developing prenatal diagnosis expertise where this is not available. Answers to some relatively simple questions about the role of the environment could also make a major difference to the management of the haemoglobin disorders. There is a major case for the development of regional networks to apply such technology as has been developed for the control and prevention of the important haemoglobin disorders, particularly in Asian countries.

Public Health Reviews

Inherited haemoglobin disorders: an increasing global health problem

D.J. Weatherall[1] & J.B. Clegg[2]

Abstract Despite major advances in our understanding of the molecular pathology, pathophysiology, and control and management of the inherited disorders of haemoglobin, thousands of infants and children with these diseases are dying through lack of appropriate medical care. This problem will undoubtedly increase over the next 20 years because, as the result of a reduction in childhood mortality due to infection and malnutrition, more babies with haemoglobin disorders will survive to present for treatment. Although WHO and various voluntary agencies have tried to disseminate information about these diseases, they are rarely mentioned as being sufficiently important to be included in setting health care priorities for the future. It takes considerable time to establish expertise in developing programmes for the control and management of these conditions, and the lessons learned in developed countries will need to be transmitted to those countries in which they occur at a high frequency.

Keywords Hemoglobinopathies/mortality/therapy/epidemiology; Anemia, Sickle cell/mortality/therapy/epidemiology; Thalassemia/mortality/therapy/epidemiology; Malaria/complications/blood; Genetic techniques; Child; Cost of illness; Forecasting (*source: MeSH*).

Mots clés Hémoglobinopathie/mortalité/thérapeutique/épidémiologie; Anémie cellule falciforme/mortalité/thérapeutique/épidémiologie; Thalassémie/mortalité/thérapeutique/épidémiologie; Paludisme/complication/sang; Technique génétique; Enfant; Coût maladie; Prévision (*source: INSERM*).

Palabras clave Hemoglobinopatías/mortalidad/terapia/epidemiología; Anemia de células falciformes/mortalidad/terapia/epidemiología; Talasemia/mortalidad/terapia/epidemiología; Paludismo/complicaciones/sangre; Técnicas genéticas; Niño; Costo de la enfermedad; Predicción (*fuente: BIREME*).

Bulletin of the World Health Organization, 2001, **79**: 704–712.

Public health reviews

Global epidemiology of haemoglobin disorders and derived service indicators

Bernadette Modell[a] & Matthew Darlison[a]

Abstract To demonstrate a method for using genetic epidemiological data to assess the needs for equitable and cost-effective services for the treatment and prevention of haemoglobin disorders. We obtained data on demographics and prevalence of gene variants responsible for haemoglobin disorders from online databases, reference resources, and published articles. A global epidemiological database for haemoglobin disorders by country was established, including five practical service indicators to express the needs for care (indicator 1) and prevention (indicators 2–5).

Haemoglobin disorders present a significant health problem in 71% of 229 countries, and these 71% of countries include 89% of all births worldwide. Over 330 000 affected infants are born annually (83% sickle cell disorders, 17% thalassaemias). Haemoglobin disorders account for about 3.4% of deaths in children less than 5 years of age. Globally, around 7% of pregnant women carry β or α zero thalassaemia, or haemoglobin S, C, D Punjab or E, and over 1% of couples are at risk. Carriers and at-risk couples should be informed of their risk and the options for reducing it. Screening for haemoglobin disorders should form part of basic health services in most countries.

Bulletin of the World Health Organization 2008;86:480–487.

Emoglobinopatie da difetto di produzione: Sindromi Talassemiche

Emoglobinopatie da difetto strutturale: Sindromi Falcemiche

Ogni anno nel mondo nascono 300.000 bambini affetti da Emoglobinopatie

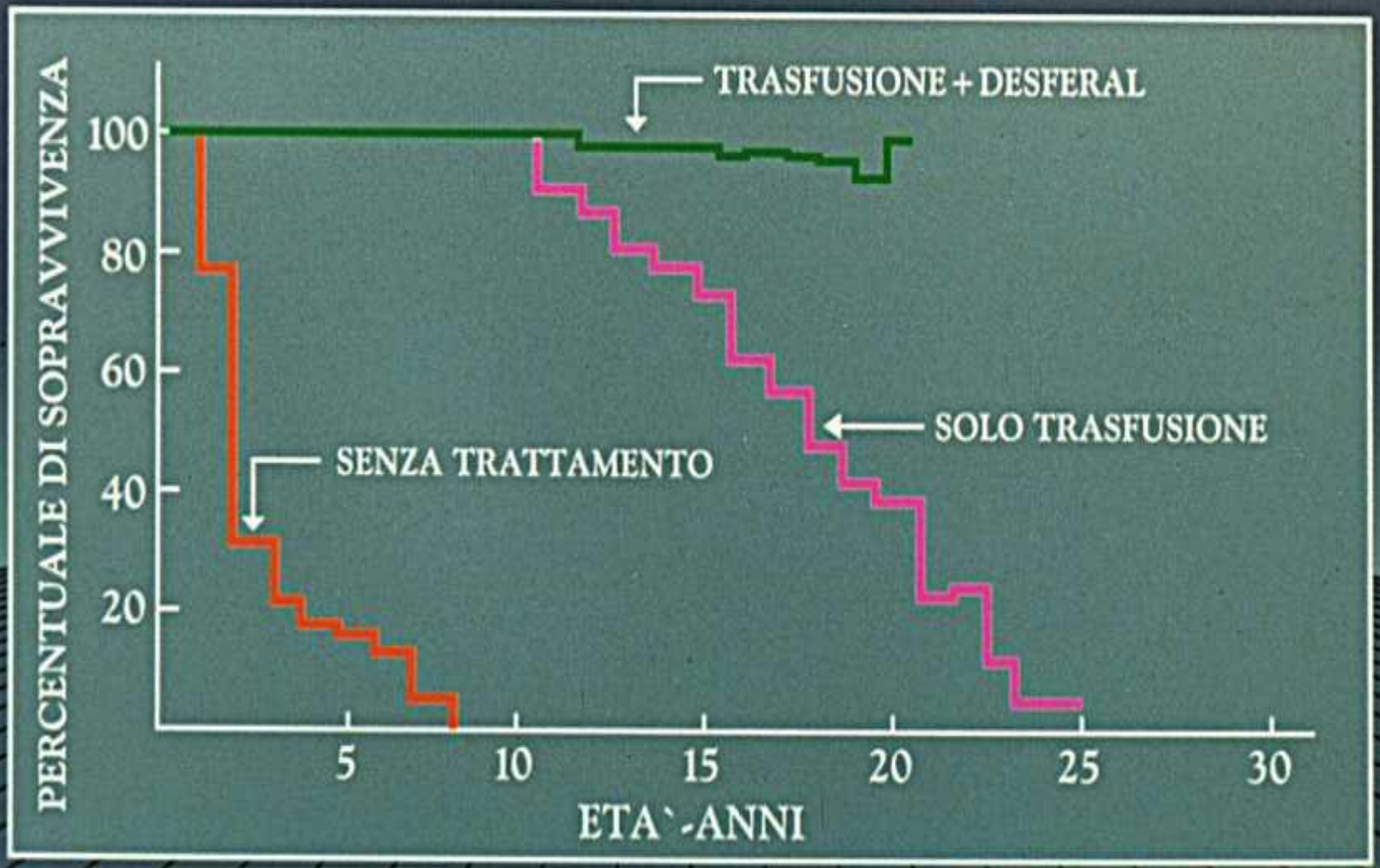
Classificazione clinica

- **Portatore sano**
- **Talassemia major (Trasfusione Dipendente)**
- **Talassemia intermedia**
- **Anemia Falciforme**

Thalassemia Major

La Thalassemia Major e' una grave forma di anemia congenita che richiede per la sopravvivenza regolari trasfusioni di globuli rossi.

(circa 250.000 unità si sangue anno)


PERCENTUALE DI SOPRAVVIVENZA
100
80
60
40
20
TRASFUSIONE + DESFERAL
SOLO TRASFUSIONE
SENZA TRATTAMENTO
5
10
15
20
25
30
ETA` -ANNI

Thalassemia Major: prognosi attuale e regime terapeutico

Quando possibile il <u>trapianto di midollo:</u>
buona possibilità di Guarigione definitiva

<u>Terapia convezionale:</u>
Prognosi aperta: senza limiti e
con buona qualità di vita

Centro Specialistico Approccio Globale

Cura del paziente thalassemico
- **Transfusione**
- **Chelazione**
- **Follow up**
- **Presa in carico psico-sociale**

Screening e consulenza ai portatori

Diagnosi Prenatale

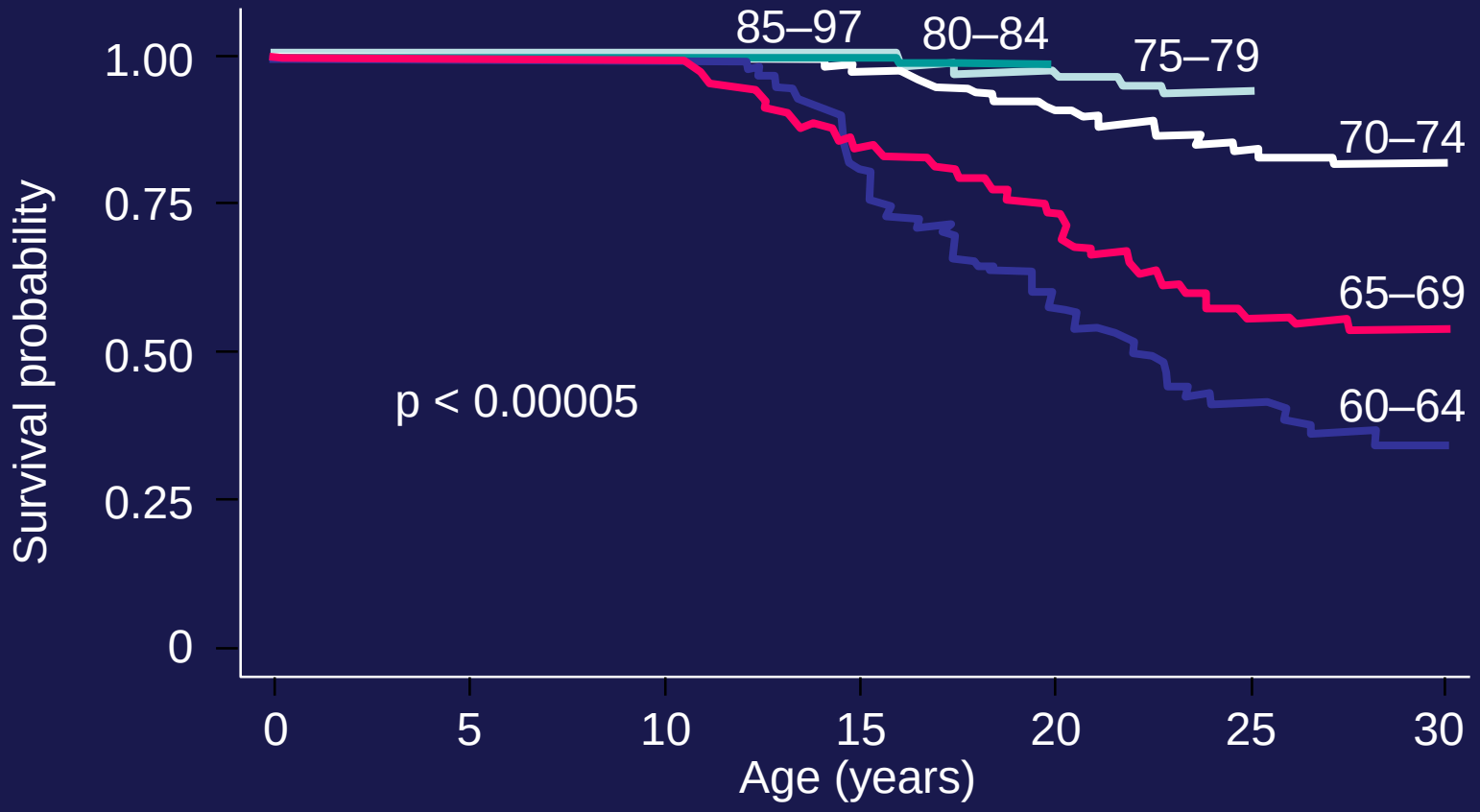
Formazione e Ricerca

Multidisciplinary Team

Specialized center

Blood Bank
Cardiologist
Endocrinologist
Diabetologist
Hepatologist
Radiologist
Transplantation Team
Gynecologist
General Surgeon
Oculist
Nephrologist
Psychologist

Miglioramento della sopravvivenza per coorte di nascita



Borgna-Pignatti C, et al. Haematologica. 2004;89:1187-93.

Cortesia MD Cappellini

Falcemia

La Falcemia é una anomalia qualitativa congenita dell'emoglobina a causa della quale i globuli rossi possono prendere la forma di una falce ed accumularsi fino a produrre blocchi della circolazione che causano crisi dolorose ed altre possibili conseguenze gravi sia sulla qualità che sull'attesa di vita.
Queste crisi possono essere scatenate da condizioni di bassa tensione di ossigeno o forti stress e sono
Tempo Dipendenti

Collana Scientifica SITE

MANAGEMENT DEL SICKLE CELL TRAIT

Buone Pratiche SITE

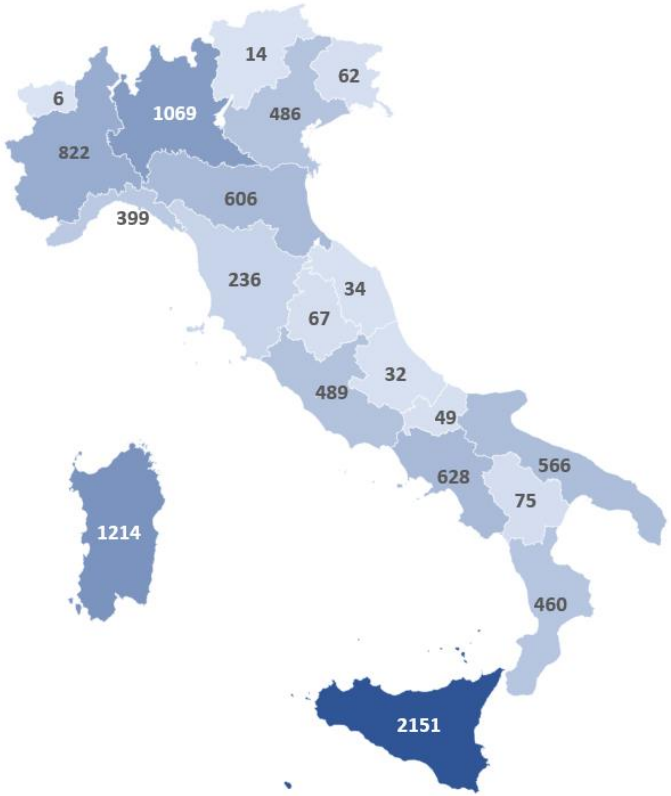
SOCIETA' ITALIANA TALASSEMIE
ED EMOGLOBINOPATIE

In partnerariato con

ASSOCIAZIONE ITALIANA EMATOLOGIA
ONCOLOGICA PEDIATRICA

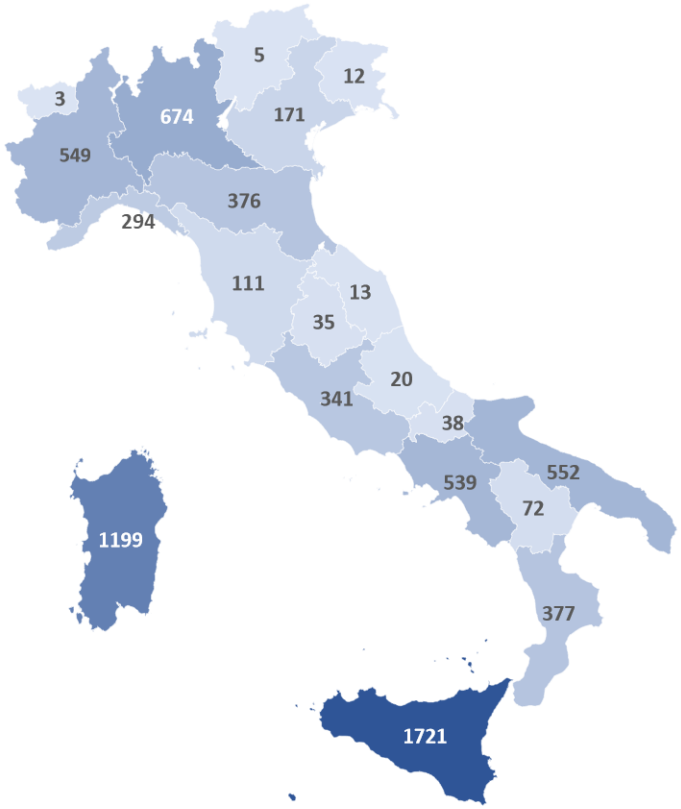
www.site-italia.org

Distribuzione Regionale dei pazienti con Emoglobinopatie

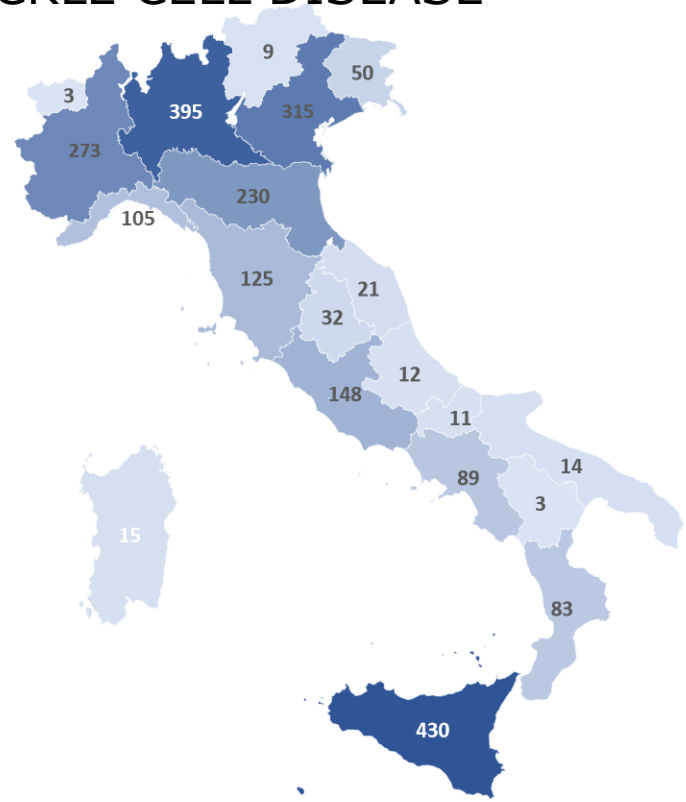


Regions	TDT	NTDT	SCD	Total
Abruzzo	8	12	12	**32**
Basilicata	72	0	3	**75**
Calabria	317	60	83	**460**
Campania	310	229	89	**628**
Emilia-Romagna	329	47	230	**606**
Friuli-Venezia-Giulia	9	3	50	**62**
Lazio	273	68	148	**489**
Liguria	164	130	105	**399**
Lombardia	381	293	395	**1069**
Marche	12	1	21	**34**
Molise	17	21	11	**49**
Piemonte	335	214	273	**822**
Puglia	488	64	14	**566**
Sardegna	827	372	15	**1214**
Sicilia	1340	381	430	**2151**
Toscana	94	17	125	**236**
Trentino Alto Adige	4	1	9	**14**
Umbria	21	14	32	**67**
Valle d'Aosta	3	0	3	**6**
Veneto	137	34	315	**486**
Total	**5141**	**1961**	**2280**	**9465**

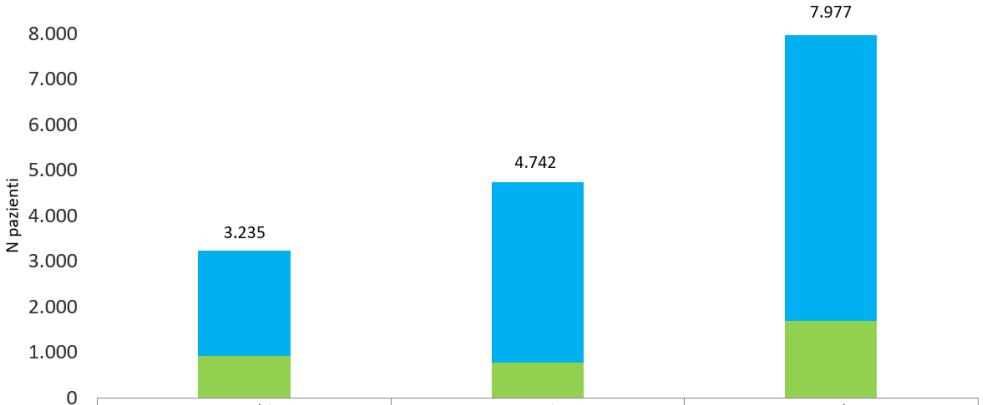
THALASSEMIA



SICKLE CELL DISEASE



Pazienti stimati con FALCEMIA in Italia nel 2018 (dati proiettati sulla popolazione nazionale)



	Maschi	Femmine	Totale
≥18 anni	2.316	3.971	6.287
<18 anni	919	771	1.690
Totale	3.235	4.742	7.977

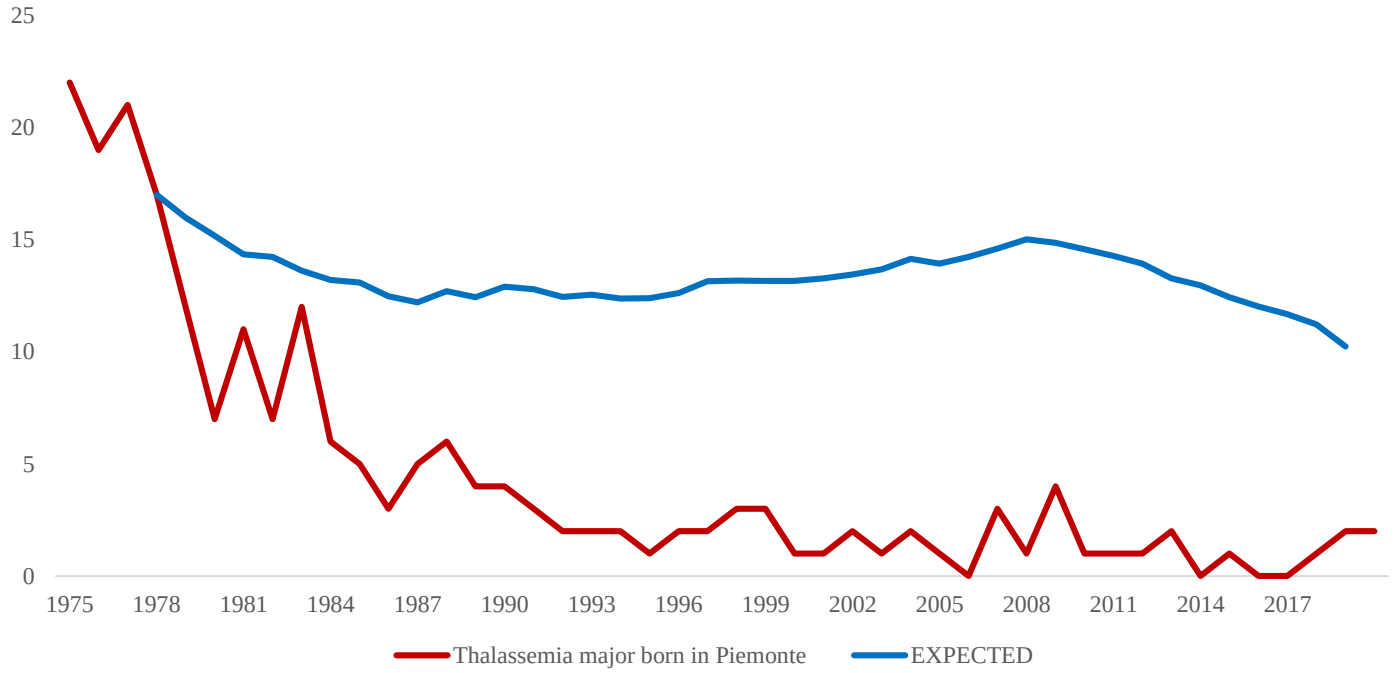
SITE 2021 – GREATalyS (CSEG101AIT01)

L'IMPATTO EPIDEMIOLOGICO DELL'ANEMIA FALCIFORME IN ITALIA: EVIDENZE DALLO STUDIO GREATALYS (GENERATING REAL WORLD EVIDENCE ACROSS ITALY IN SCD)

L. De Franceschi1, G.L. Forni2, C. Castiglioni3, C. Condorelli3, D. Valsecchi3, E. Premoli3, V. Perrone4, L. Degli Esposti4, C. Fiocchi3 in rappresentanza del gruppo dello studio GREATalyS

1Department of Medicine, University of Verona, Italy, 2Centro della Microcitemia e Anemie Congenite, Ospedale Galliera, Genoa, Italy, 3Novartis Farma S.p.A., Origgio, Italy, 4CliCon Srl, Health, Economics & Outcomes Research, Bologna, Italy.

Reduction of Birth Rate for Thalassemia in Piemonte since the Application of Screening and Prenatal Diagnosis (1978) (updated on Aug 02, 2017)



Thalassemia Centre
University of Torino

OPERA PIA DE FERRARI BRIGNOLE SALE II

OSPEDALI GALLIERA

ESTRATTO

dal verbale delle Deliberazioni prese dal Consiglio di Amministrazione

nelle sedute dal 3 Luglio 1963

O M I S S I S

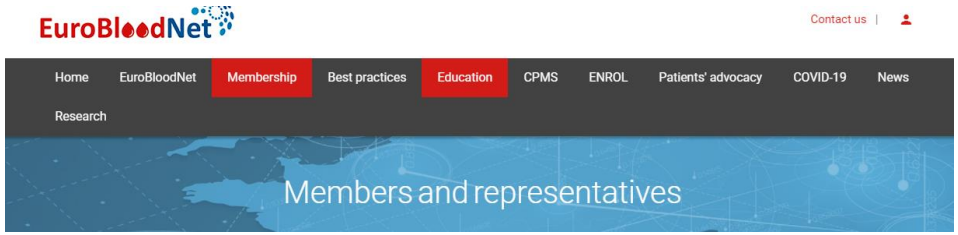
ISTITUZIONE DEL CENTRO DI MEDICINA SOCIALE PER LA PROFILASSI, LA DIAGNOSI E LA CURA DELLE TALASSIEMIE, DEL MORBO DI COOLEY E DELL'ANEMIA MICROSFEROCITOSICA -

Distribuzione dei centri per la cura delle TALASSEMIE e delle ANEMIE FALCIFORMI

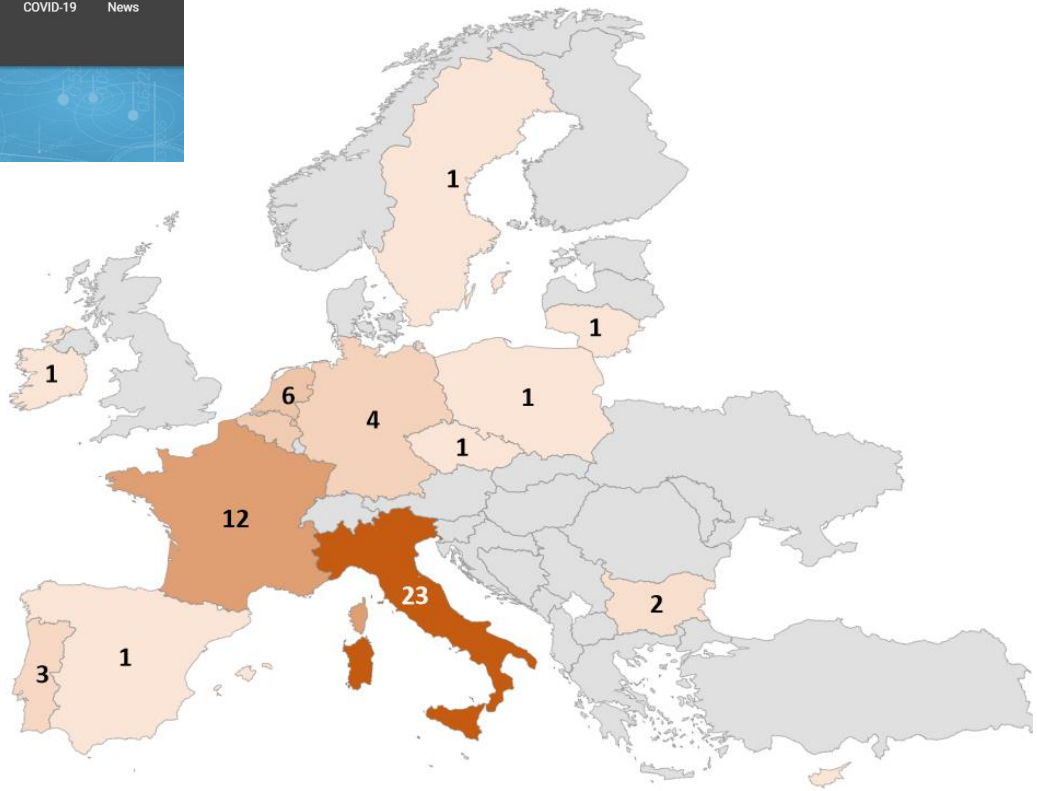
Survey SITE

https://centri-site-italia.org

- 131 hanno risposto al censimento
- 46 non compaiono come centri afferenti alla rete delle malattie rare – circa 1500 pazienti seguiti in questi centri



Stato	Numero di Centri ERN
Italia	23
Francia	12
Paesi Bassi	6
Belgio	5
Germania	4
Portogallo	3
Bulgaria	2
Cipro	1
Irlanda	1
Lituania	1
Polonia	1
Spagna	1
Svezia	1
Repubblica Ceca	1
Totale	**62**

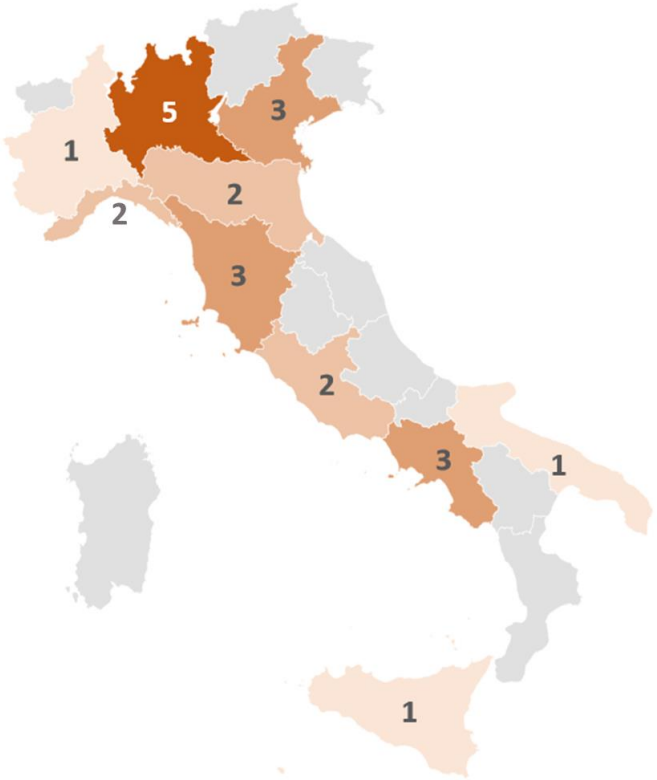


23/62 (37%) centri ERN sono Italiani

https://eurobloodnet.eu/members/representative/
Ultimo accesso 01/07/2021

Distribuzione dei centri ERN EuroBloodNet in Italia

Regione	Città	N. Centri ERN
Campania	Napoli	3
Lazio	Roma	2
Liguria	Genova	2
Lombardia	Bergamo	1
Lombardia	Milano	2
Lombardia	Monza	1
Lombardia	Pavia	1
Piemonte	Torino	1
Puglia	Bari	1
Emilia Romagna	Modena	1
Emilia Romagna	Ferrara	1
Sicilia	Palermo	1
Toscana	Firenze	1
Toscana	Pisa	1
Toscana	Siena	1
Veneto	Padova	1
Veneto	Verona	1
Veneto	Vicenza	1
Totale		**23**



Il 70% (16/23) dei centri ERN Italiani sono specializzati nel trattamento delle emoglobinopatie

Prospettive alla luce dei nuovi approcci terapeutici

Riduzione o eliminazione della necessità trasfusionale
Il paziente talassemico adulto/anziano tale rimarrà anche se potrà accedere a queste terapie

Nuovi approcci trapeutici

Stimolatori della Eritropiesi (1 Farmaco approvato EMA)

Terapia Genica (1 Farmaco approvato EMA)

Chi le prescriverà?

HemaSphere
Powered by EHA

EHA EUROPEAN HEMATOLOGY ASSOCIATION

Guideline Article - Expert opinion

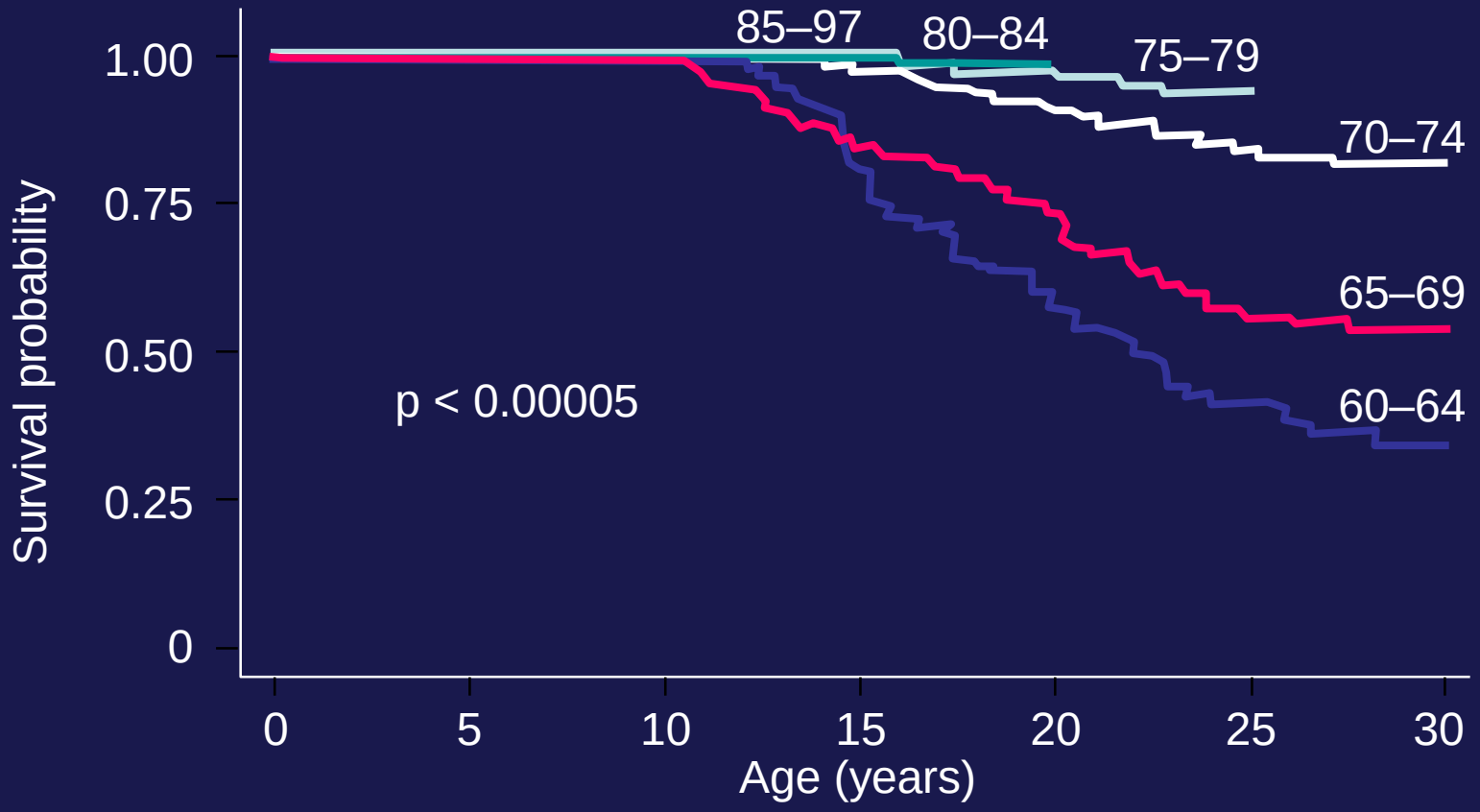
OPEN ACCESS

Selecting β-thalassemia Patients for Gene Therapy: A Decision-making Algorithm

Donatella Baronciani[1], Maddalena Casale[2], Lucia De Franceschi[3], Giovanna Graziadei[4], Filomena Longo[5], Raffaella Origa[6], Paolo Rigano[7], Valeria Pinto[8], Monia Marchetti[9], Antonia Gigante[10], Gian Luca Forni[8]

A consensus document originally developed by an expert panel of the Italian Society of Thalassemias and Hemoglobinopathies (SITE), reviewed and adopted by the European Hematology Association (EHA) through the EHA Scientific Working Group on Red Cells and Iron

Miglioramento della sopravvivenza per coorte di nascita

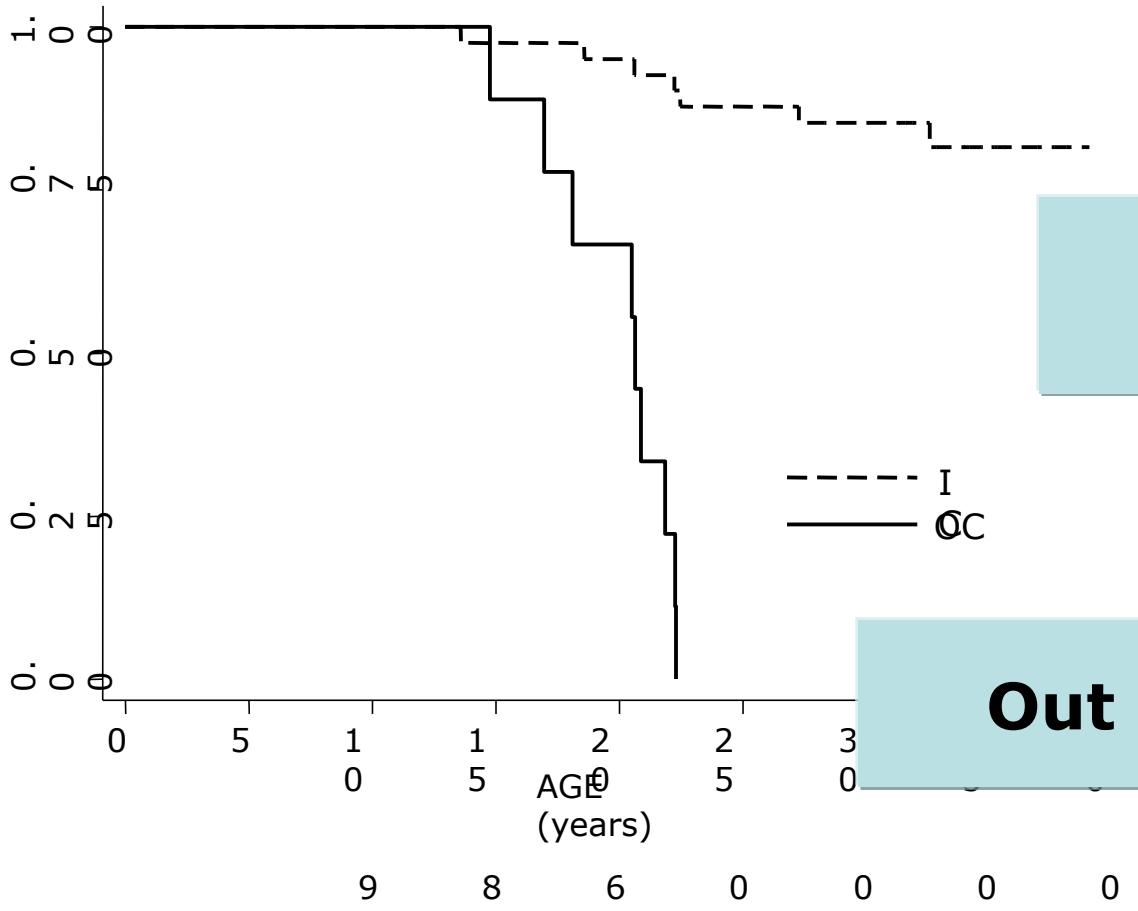


Borgna-Pignatti C, et al. Haematologica. 2004;89:1187-93.

Am J Hematol. 2009 May;84(5):317-8.

The influence of treatment in specialized centers on survival of patients with thalassemia major

Forni GL, Puntoni M, Boeri E, Terenzani L, Balocco M.



In center

Out center