I problemi del bambino migrante: I contesti clinici e assistenziali

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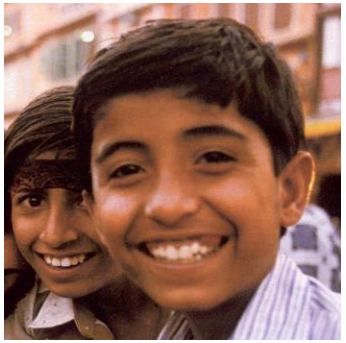
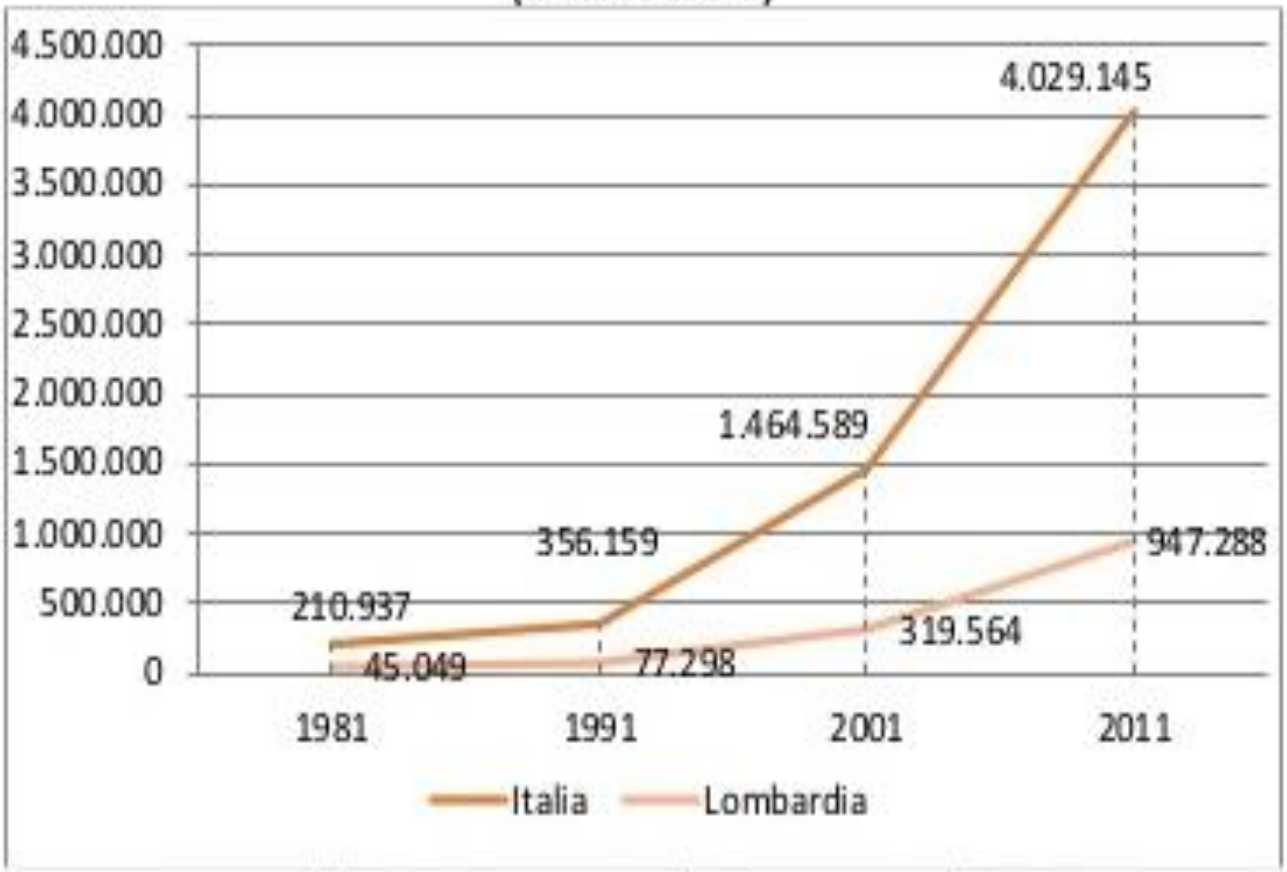
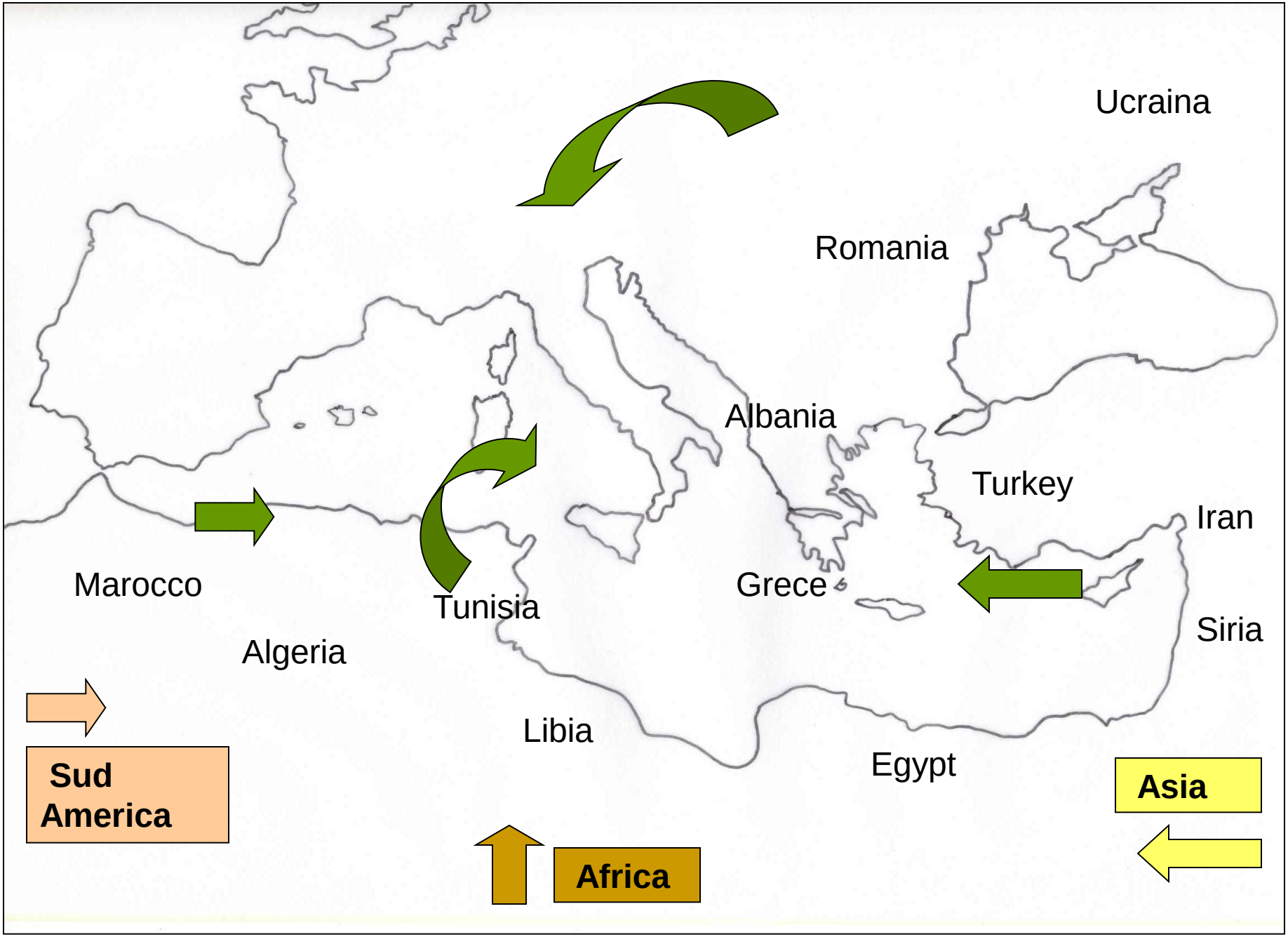


Grafico 1: Evoluzione della presenza degli stranieri in Italia e in Lombardia alle date dei censimenti (anni 1981-2011)



Fonte: Elaborazioni Excursus su dati ISTAT, www.dati.istat.it


Ucraina
Romania
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Iran
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Tunisia
Grece
Siria
Algeria
Libia
Egypt
Sud America
Asia
Africa

I contesti clinici: le anemie

Possibili eziologie per meccanismo patogenetico

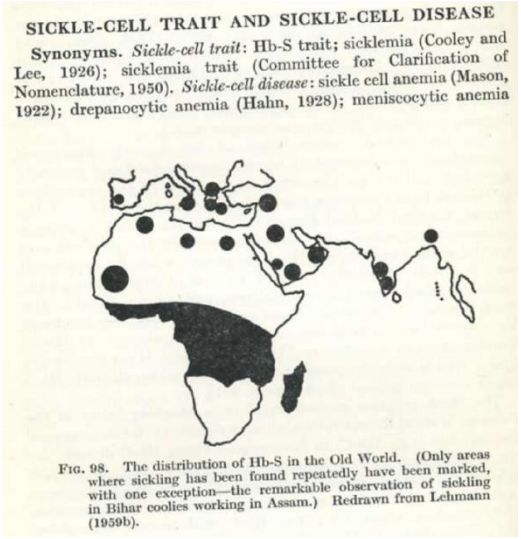
Emolisi: malaria
(deficit di G6PDH e terapia antimalarica con primachina)

Perdita: protozoi intestinali: *Entamoeba hystolitica*
elmintiasi: hookworms
Trichiuris trichiura
schistosomiasi in fase acuta

Carenziale: malnutrizione
malassorbimento (deficit vit. B12 in giardiasi;
sprue tropicale)

Inibizione/infiltrazione midollare: tubercolosi
leishmaniosi viscerale
HIV

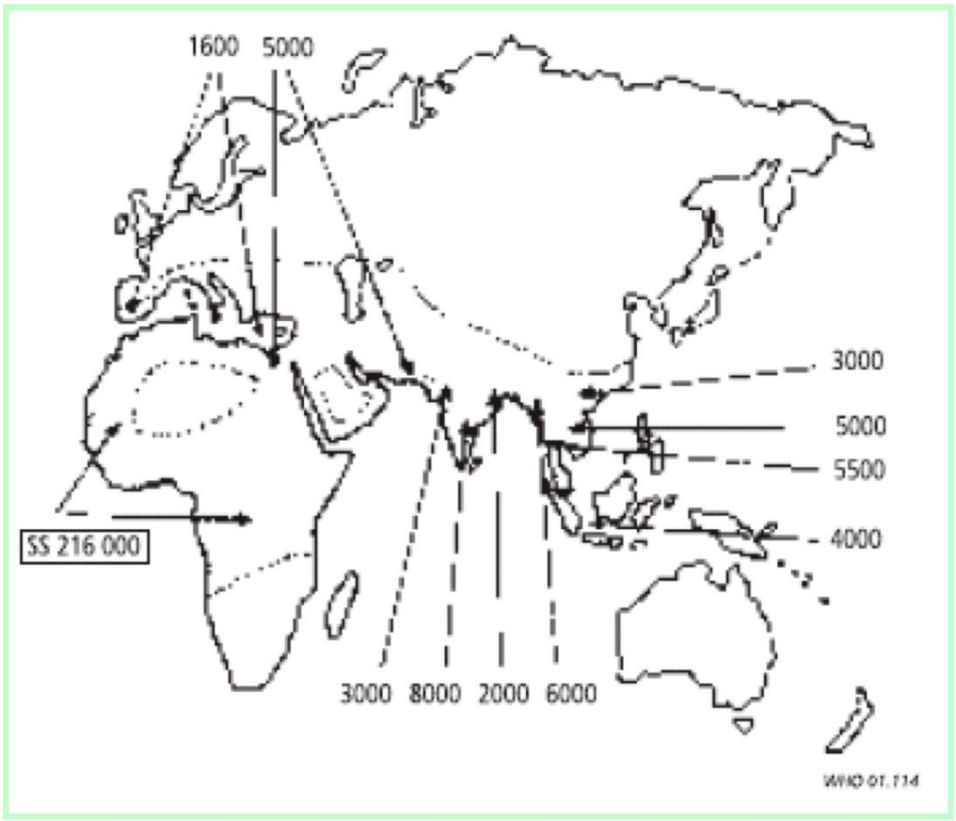
SCD as emerging problem of public health in non endemic areas



SICKLE-CELL TRAIT AND SICKLE-CELL DISEASE

Synonyms. *Sickle-cell trait*: Hb-S trait; sicklemia (Cooley and Lee, 1926); sicklemia trait (Committee for Clarification of Nomenclature, 1950). *Sickle-cell disease*: sickle cell anemia (Mason, 1922); drepanocytic anemia (Hahn, 1928); meniscocytic anemia

FIG. 98. The distribution of Hb-S in the Old World. (Only areas where sickling has been found repeatedly have been marked, with one exception—the remarkable observation of sickling in Bihar coolies working in Assam.) Redrawn from Lehmann (1959b).



Weatherall DJ et al. Bulletin WHO 79: 704, 2001;
Modell B et al Bulletin WHO 86: 480, 2008

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

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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.

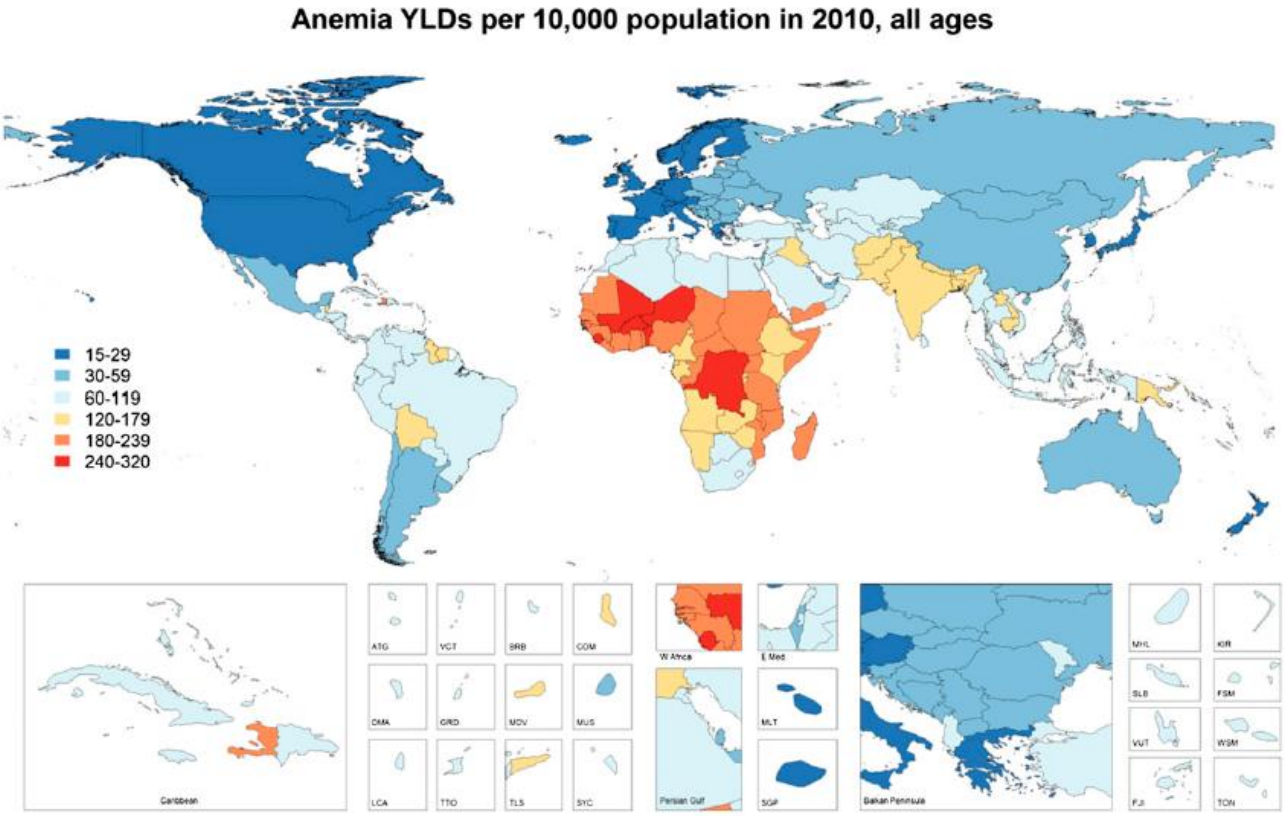
Bulletin of the World Health Organization 2008;86:480–487.

Worldwide Status of Hemoglobin disorders

- 270 million carriers of Hb disorders:

  80000 of Thalassaemia, most of Sickle Cell Disease.
- 300000 affected births per year total.
- 60-70000 births of Thalassaemics: most of these die in early life, often with no diagnosis and no or inadequate treatment.
- About 200000 new cases of SCD per year.

Hemoglobinopathies are Emerging Problem of Public Health based on YLD and DALYs (1999-2010; 2010-2055)



YLDs: years lived with disability for **hemoglobinopathies** (**β-thal and SCD**): **10.197** *vs* 21.342 cardiovascular disorders

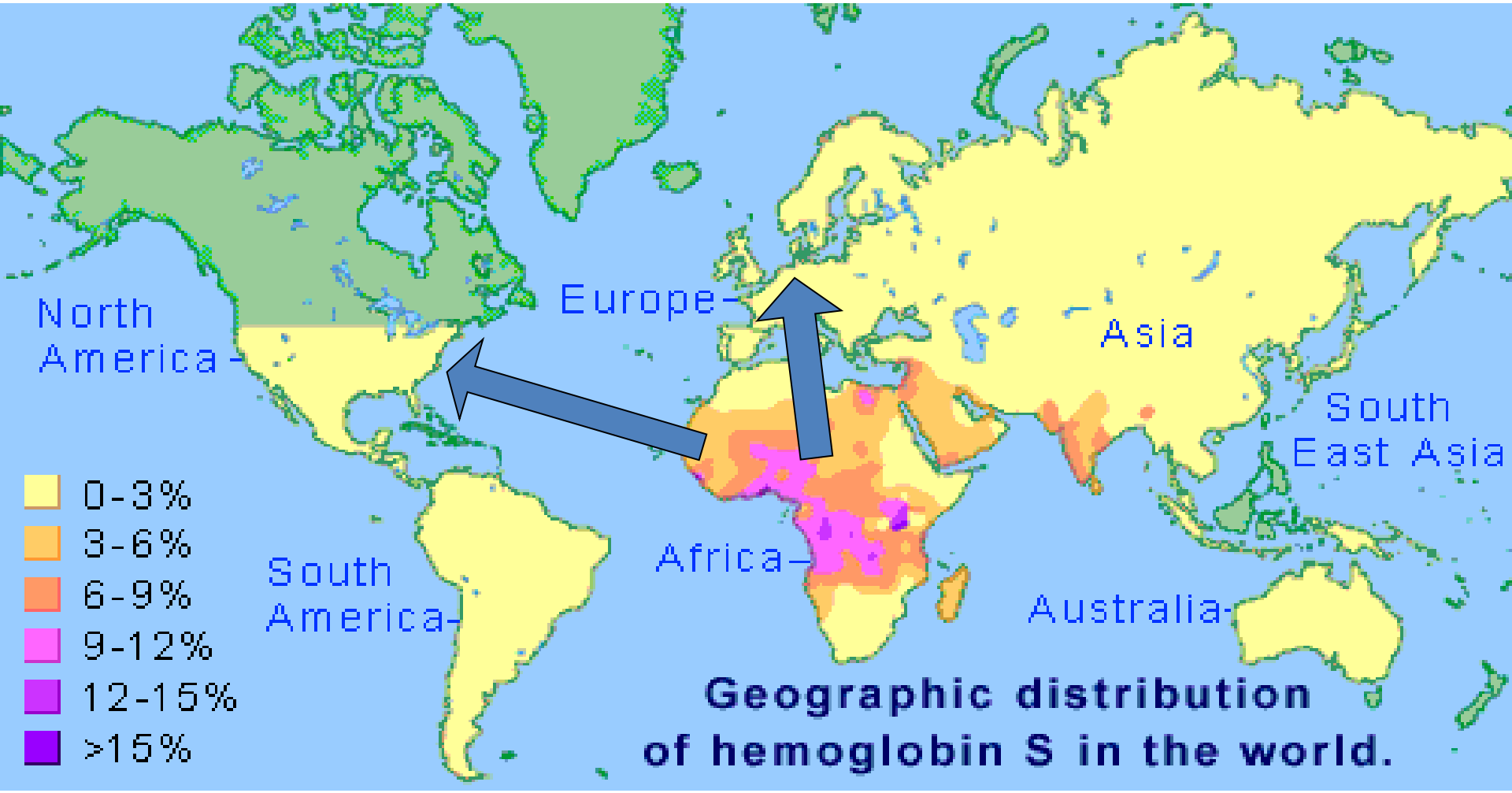
DALYs: disability adjusted life years for **hemoglobinopathies** (**β-thal and SCD**): **15.640** *vs* 75.000 diabetes

Murray CJ et al Lancet 380: 2197, 2012; Kassebaum NJ Blood 123: 615, 2014

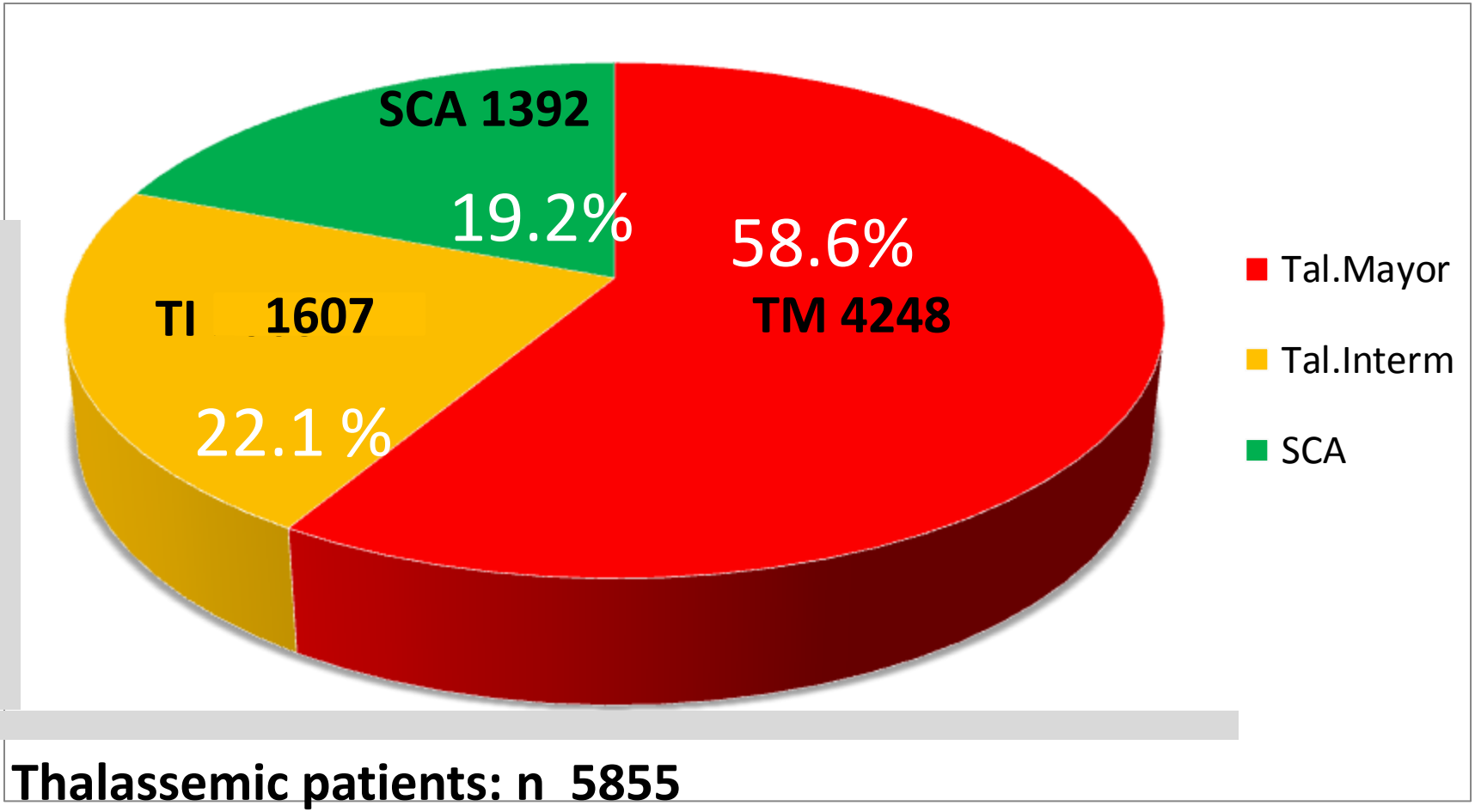
Ghana

Waiting at Sickle Cell Clinic, KATH

SCD is now a global disease



Patients with Hemoglobinophaties in Italy: 7.247

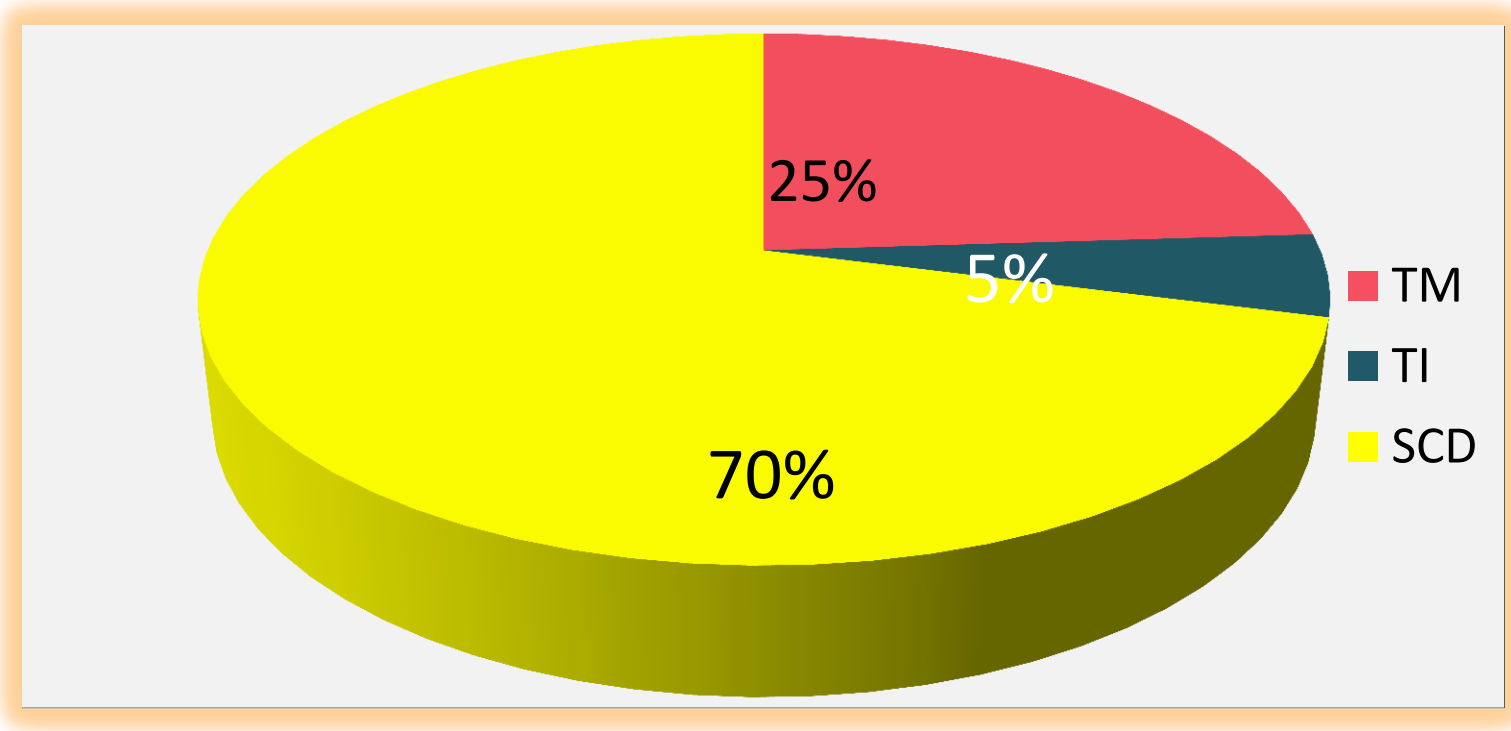


Thalassemic patients: n 5855

SCA patients: n 1391

SITE data -2010 yr

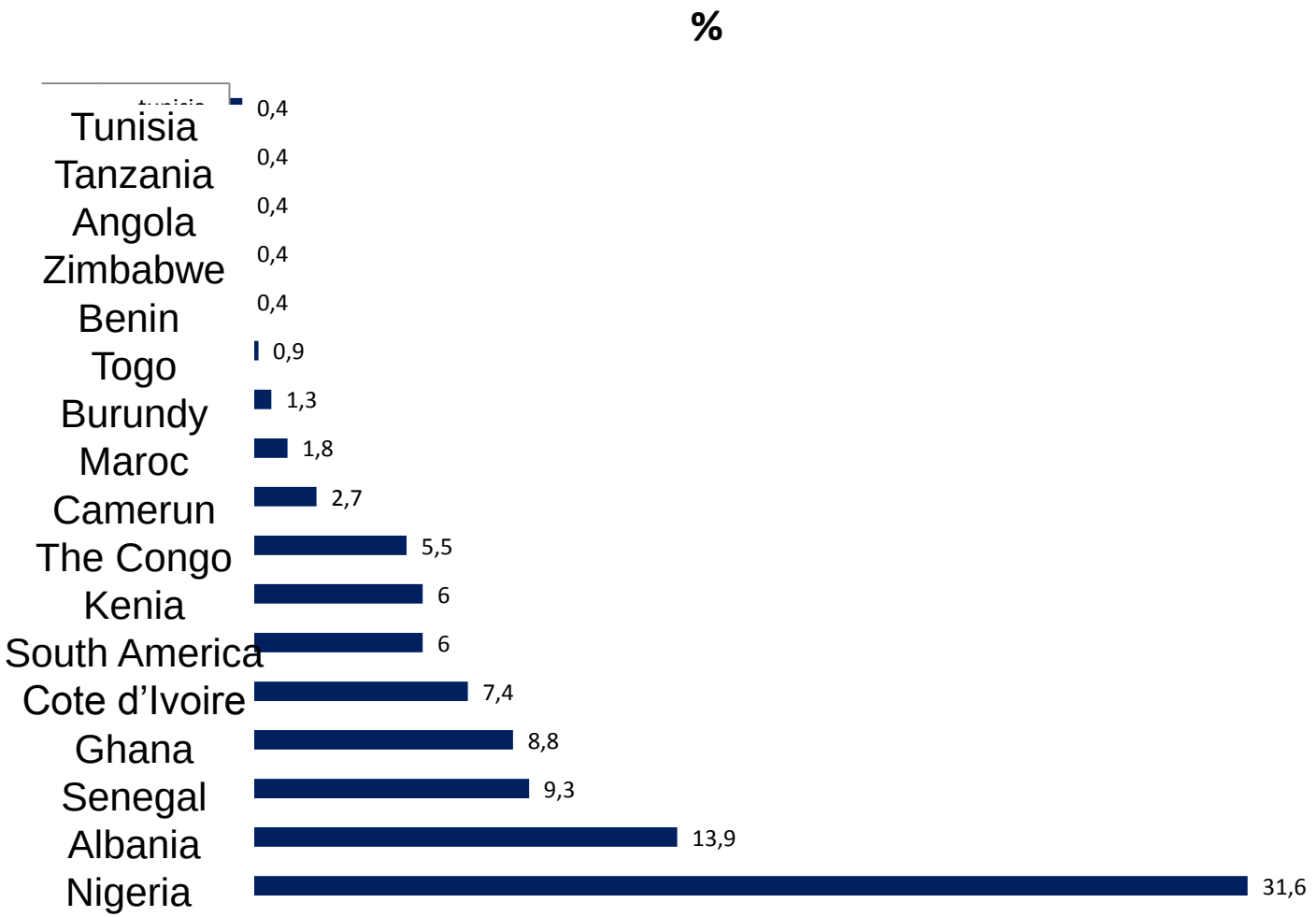
Immigrants and diseases (%)



SITE data -2010 yr

SCA and immigration-flows:national census

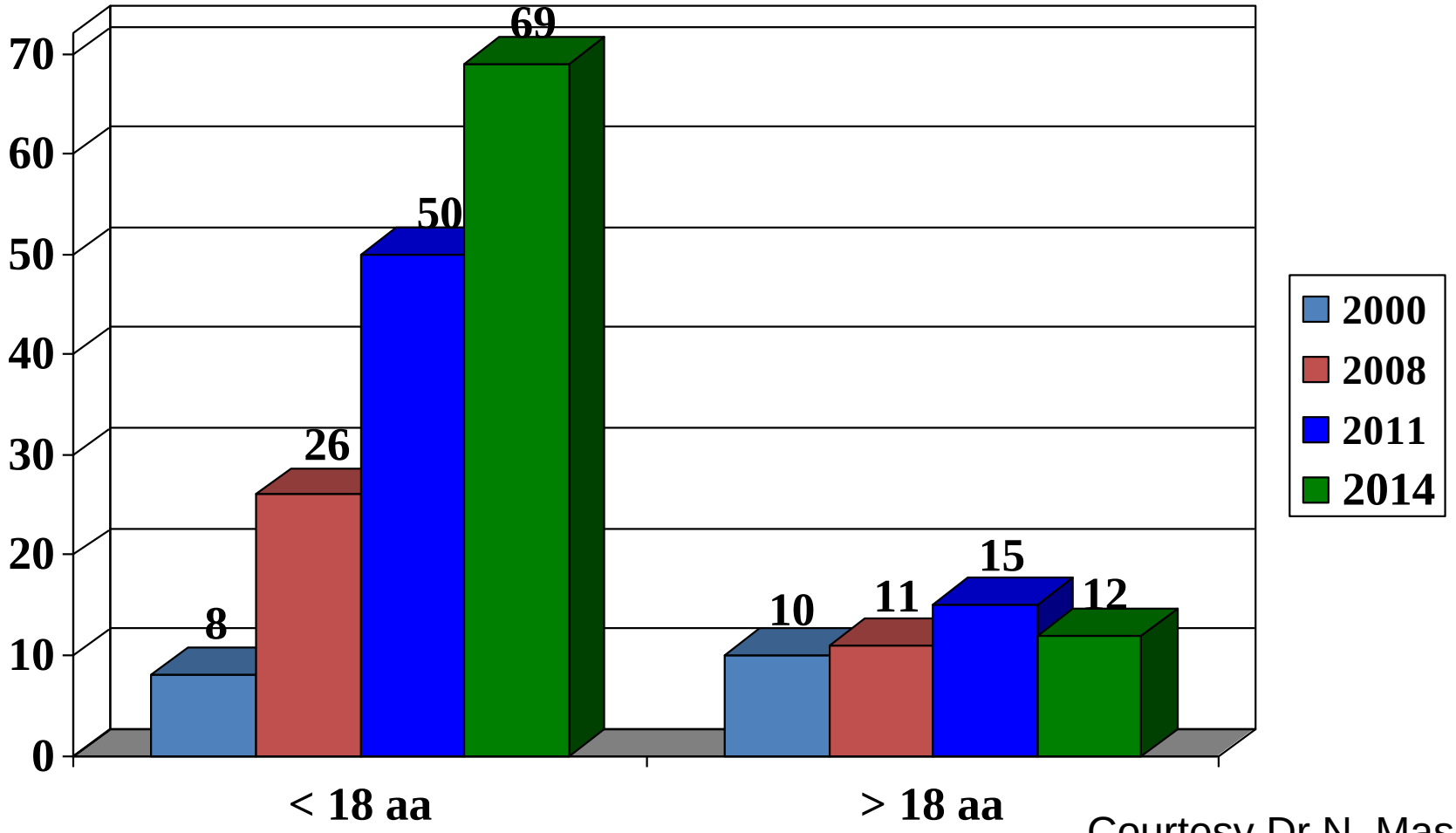
Survey carried out on 225 immigrant patients



Today SCA in Italy is " imported " from Africa and Albania

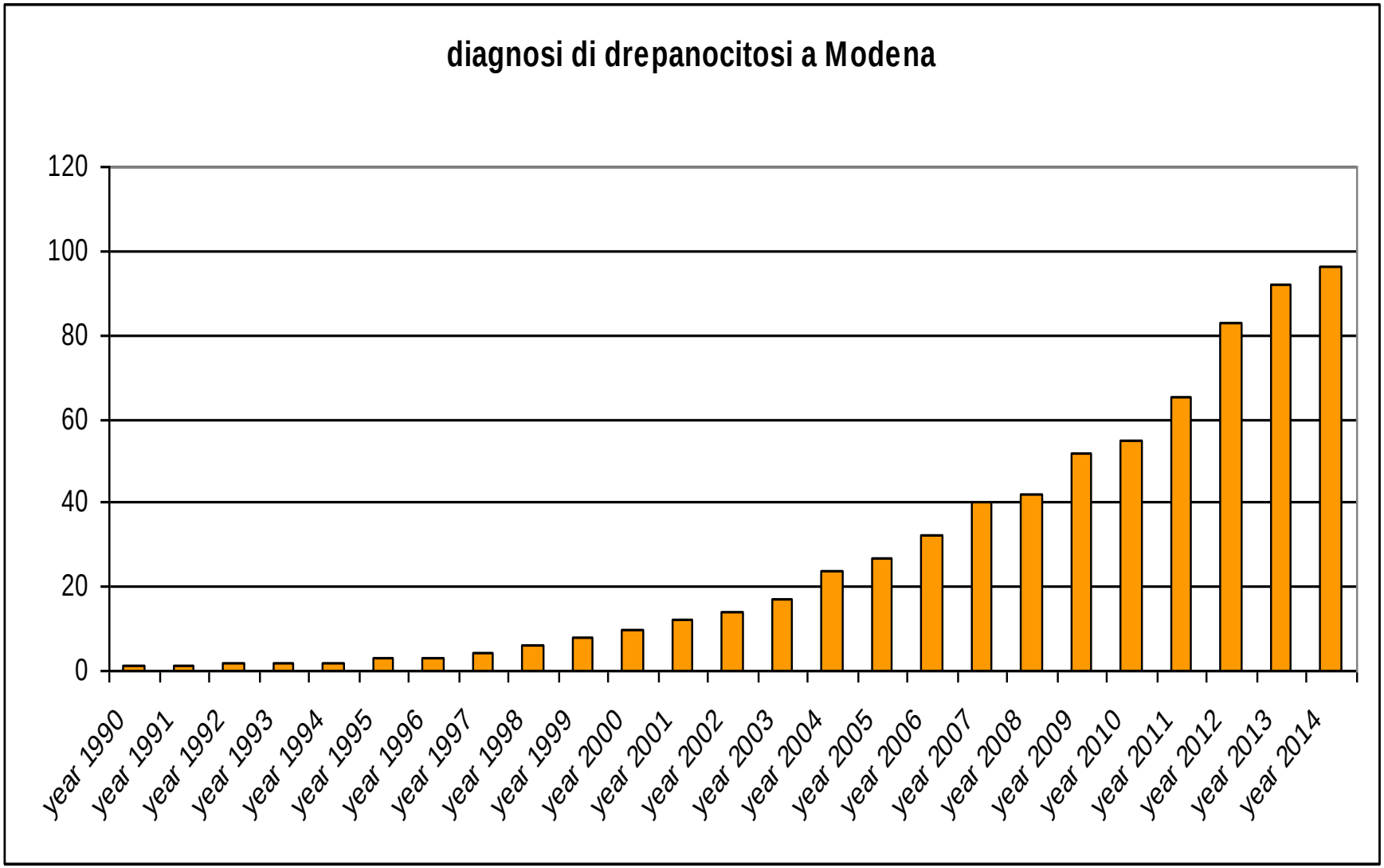
SITE CENSUS 2010

Monza Ematologia Pediatrica: incremento casi SCD da dicembre 2000 a dicembre 2014

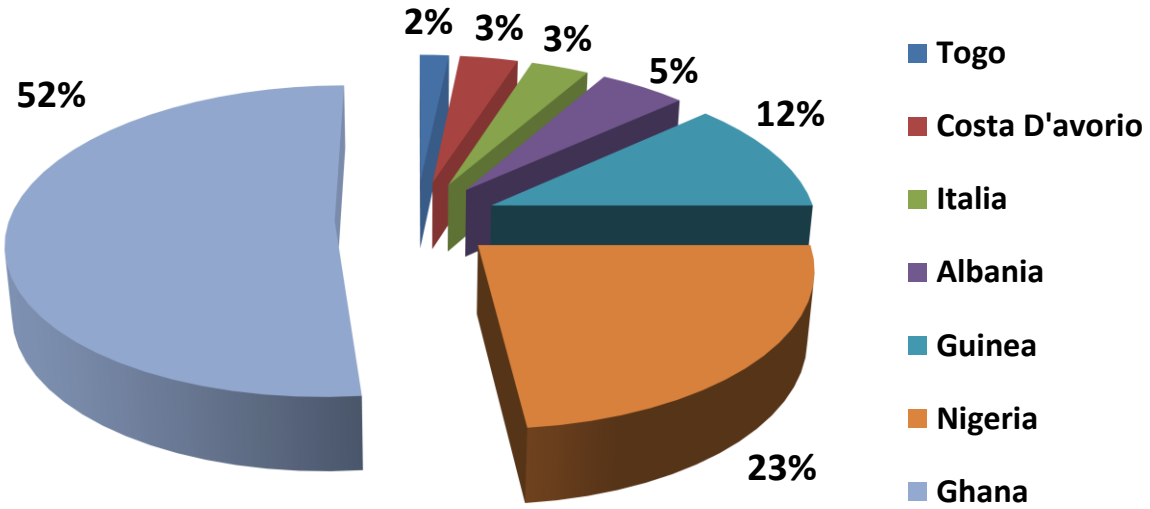


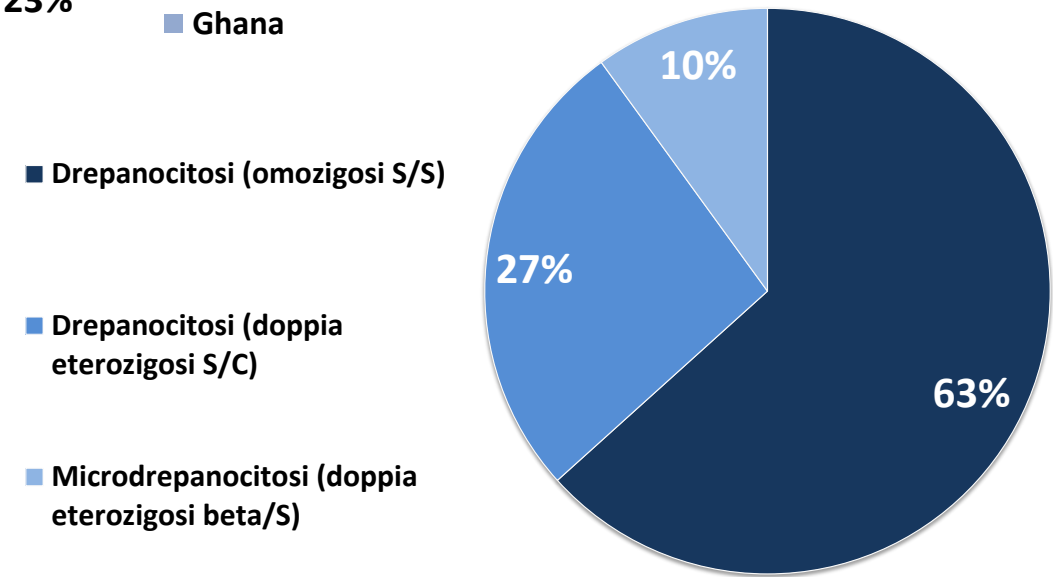
Courtesy Dr N. Masera

DIAGNOSI DI SCD 1990-2014 NELLA U.O. di PEDIATRIA Del POLICLINICO di MODENA



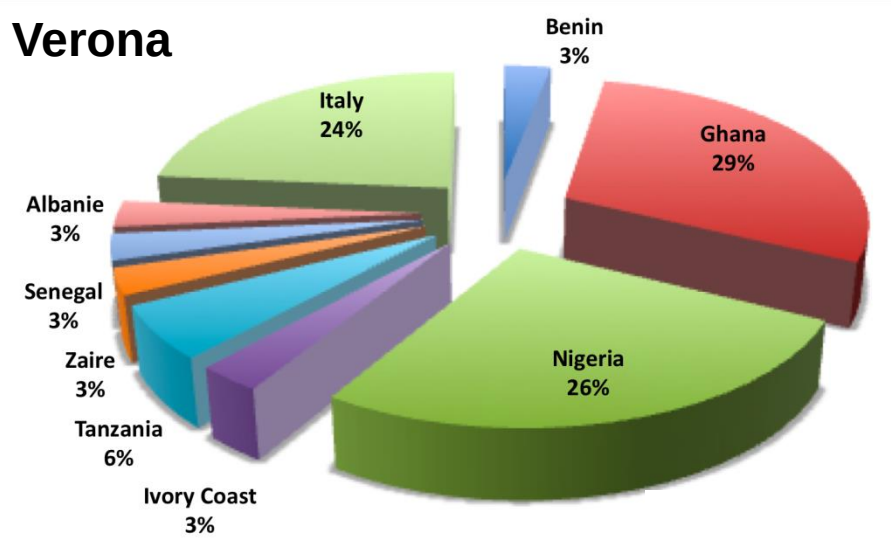
DISTRIBUZIONE DELLE VARIANTI DI SCD DIAGNOSTICATE PRESSO L'U.O. DI ONCOEMATOLOGIA PEDIATRICA DI MODENA E PROVENIENZA DEI PAZIENTI



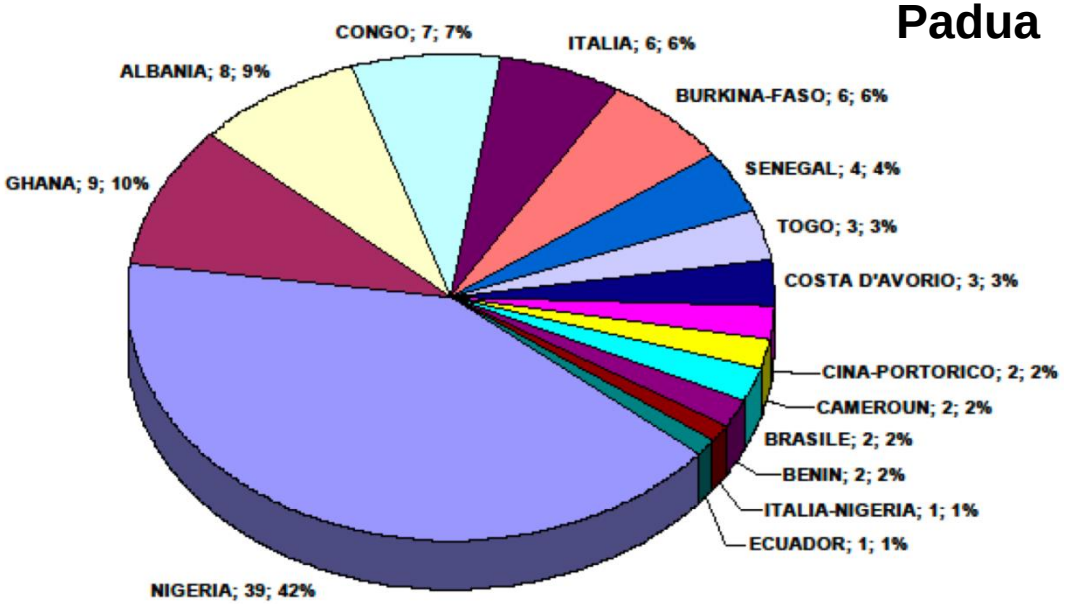


Countries of Origin of SCD Children

Verona



Padua

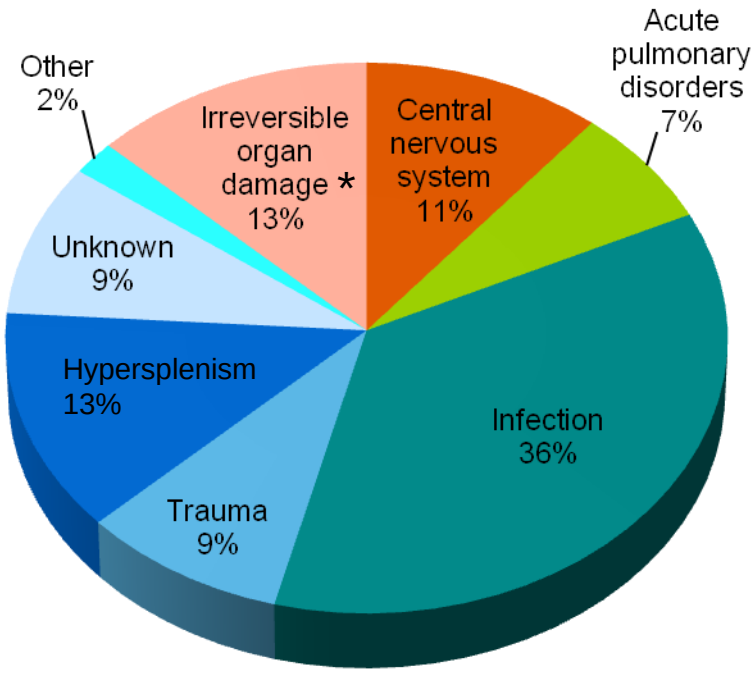


Oncoematologia Pediatrica, AUOI Verona

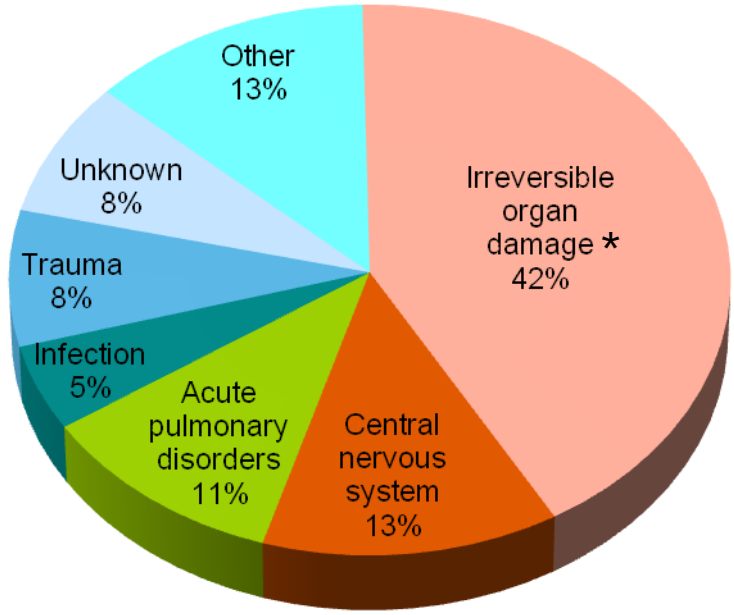
Sickle Cell Group, Clinica di Oncoematologia Pediatrica, Padova

I contesti clinici: i problemi

Cause of death in children versus adults



< 20 years of age (n = 46)



≥ 20 years of age (n = 186)

*Lung, kidney, and/or liver.

Powers DR, et al. Medicine. 2005 ;84:363-75.

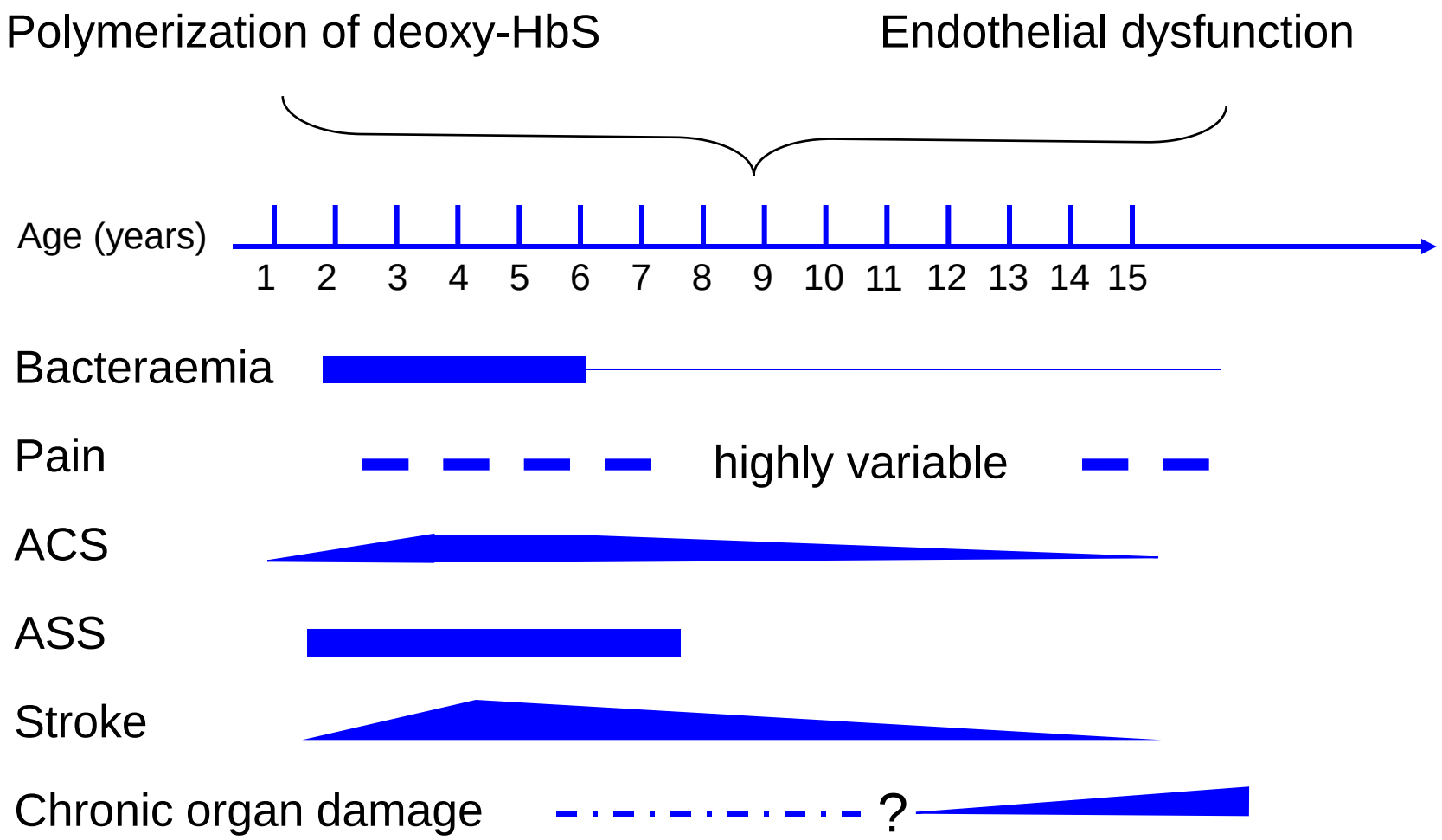
Causes of death in children with SCD

	Year (range)	Country	Incidence	Causes
Gill	1978–98	USA	1.1/100 pt-yr	11 sepsis (9 S.pn), 2 ASS, 1 CVA
Thomas	1985–92	France (Paris)	0.29%/yr	15 sepsis (8 S.pn), 3 ASS, 3 CVA
Quinn	1983–04	USA (Texas)	0.59/100 pt-yr	5 sepsis (4 S.pn), 3 ACS, 2 multi-organ failure, 1 CVA, 1 myocardial infarct
Quinn	1983–05	USA (Texas)	0.52/100 pt-yr	5 ACS, 4 multi-organ failure, 4 S.pn sepsis

CVA = cerebrovascular accident; pt-yr = patient years;
S.pn = Streptococcus pneumoniae.

Gill FM, et al. Blood. 1995;86:776-83.
Thomas C, et al. Arch Pediatr. 1996;3:445-51.
Quinn CT, et al. Blood. 2004;103:4023-7.
Quinn CT, et al. Blood. 2010;115:3447-52.

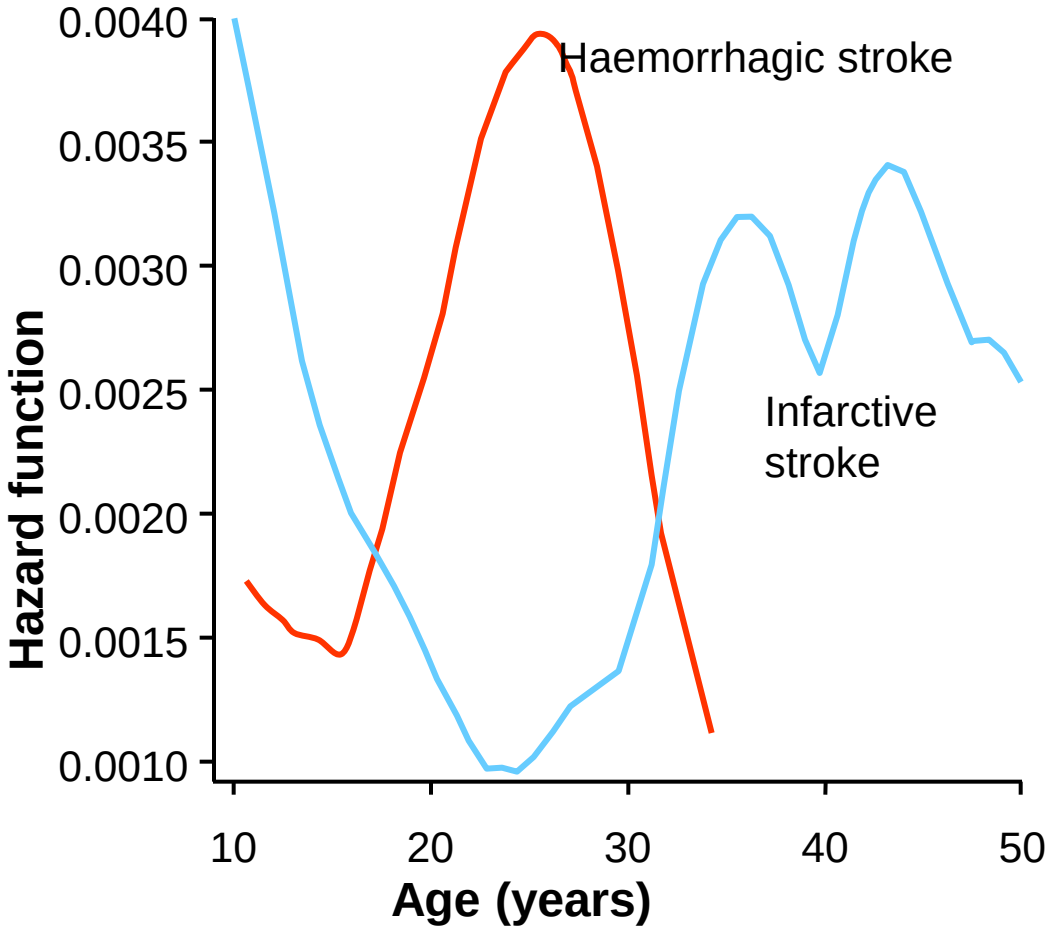
Complications of SCD in children



ASS = acute splenic sequestration.

Castro O, et al. Blood. 1994;84:643-9.
Gill FM, et al. Blood. 1995;86:776-83.
Ohene-Frempong K, et al. Blood. 1998;91:288-94.

Stroke subtype by age

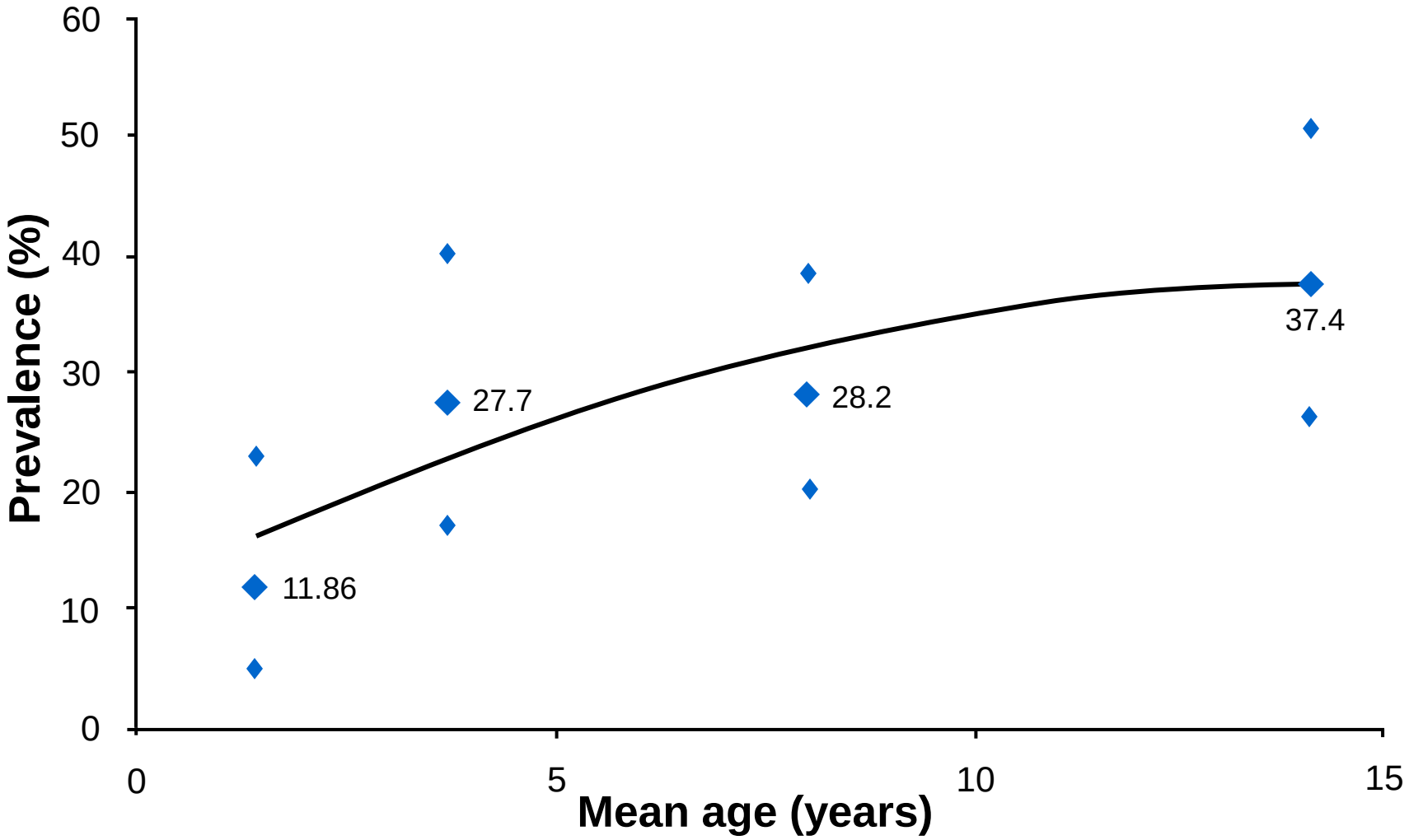


- **Ischaemic stroke**
  - 54% of CVAs
  - highest in 1st decade and after 30 years
  - peak at 2–5 years
- **Haemorrhagic stroke**
  - during 2nd decade
  - Risk factors: low Hb, high WBC, hypertension and steroids use
- **Silent stroke**
  - radiological findings consistent with white-matter disease
  - 10–30% (not characterized as age-dependent)
  - associated with cognitive deficiencies and higher stroke risk

CVA = cerebrovascular accident.

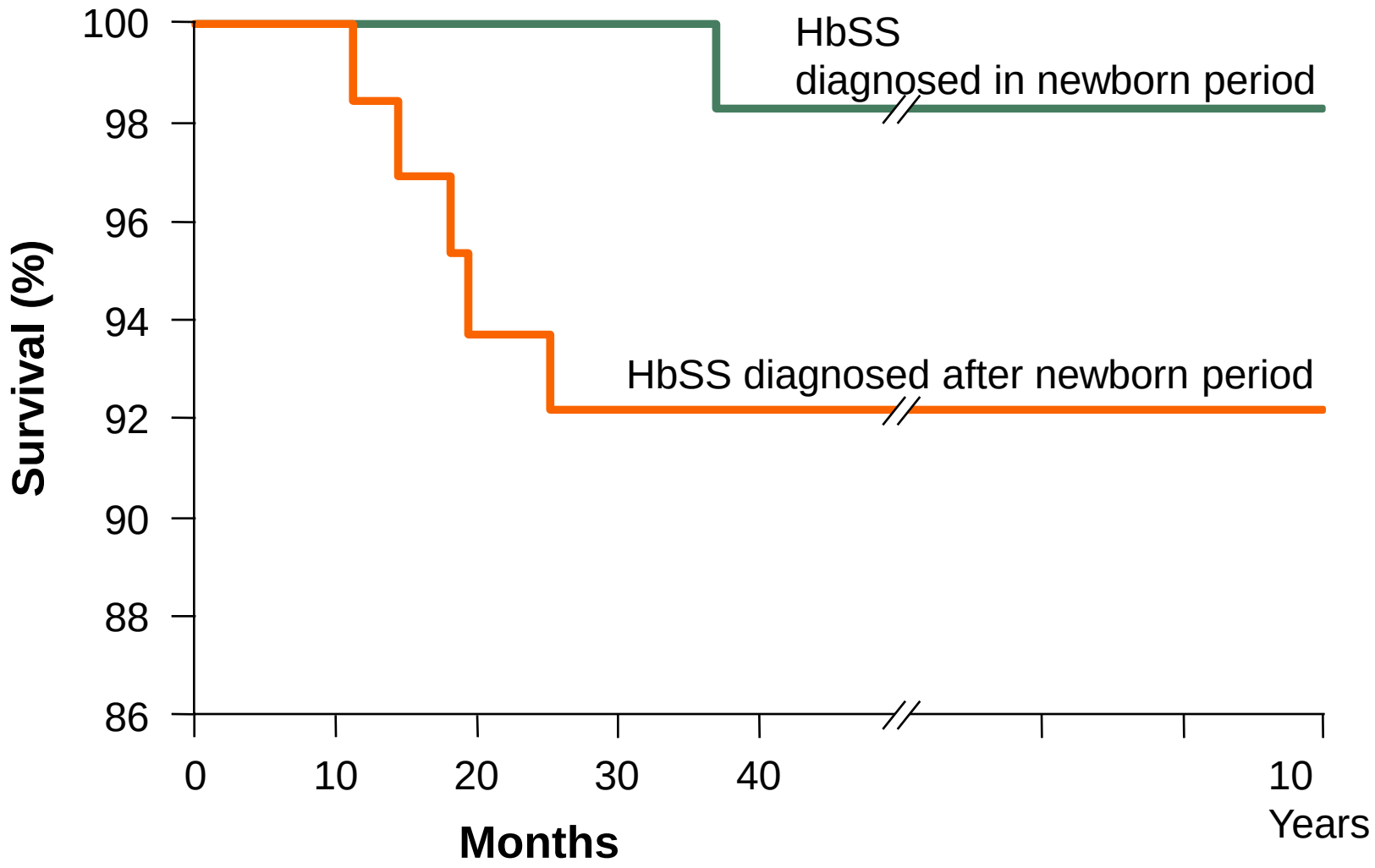
Verduzco LA, Nathan DG. Blood. 2009;114:5117-25.

Prevalence of silent infarcts



DeBaun MR, et al. Blood. 2012;119:4587-96.

Earlier diagnosis positively impacts survival



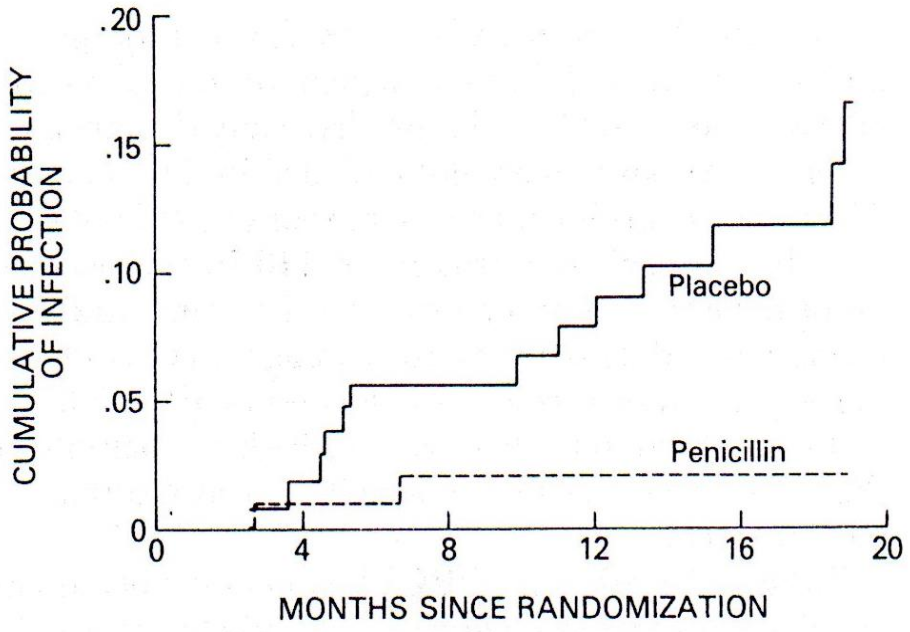
HbSS = haemoglobin SS.

Vichinsky E, et al. Pediatrics. 1988;81:749-55.

STUDI SU PROFILASSI E INFEZIONI

Prophylaxis with Oral Penicillin in Children with Sickle Cell Anemia. Gaston MD, Marilyn H. N Engl J Med 1986; 314:1593-1599 June 19 1986

The NEW ENGLAND JOURNAL of MEDICINE



Lo studio ha dimostrato

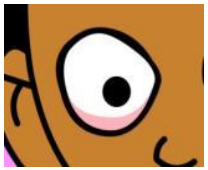
la **riduzione dell'84% nell'incidenza di infezioni** da S. Pneumoniae nei bambini con SCD in profilassi orale con penicillina, rispetto a quelli che non avevano ricevuto il trattamento

La profilassi dovrebbe essere iniziata in tutti i neonati **entro i 3 mesi di vita** alla dose di 125 mg due volte al giorno per os e incrementata a 250 mg due volte a giorno dall'età di 3 anni fino ai 5 anni

Education of patients

What to do in case of pain?

+



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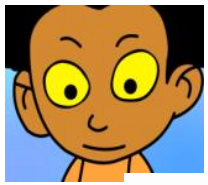

or

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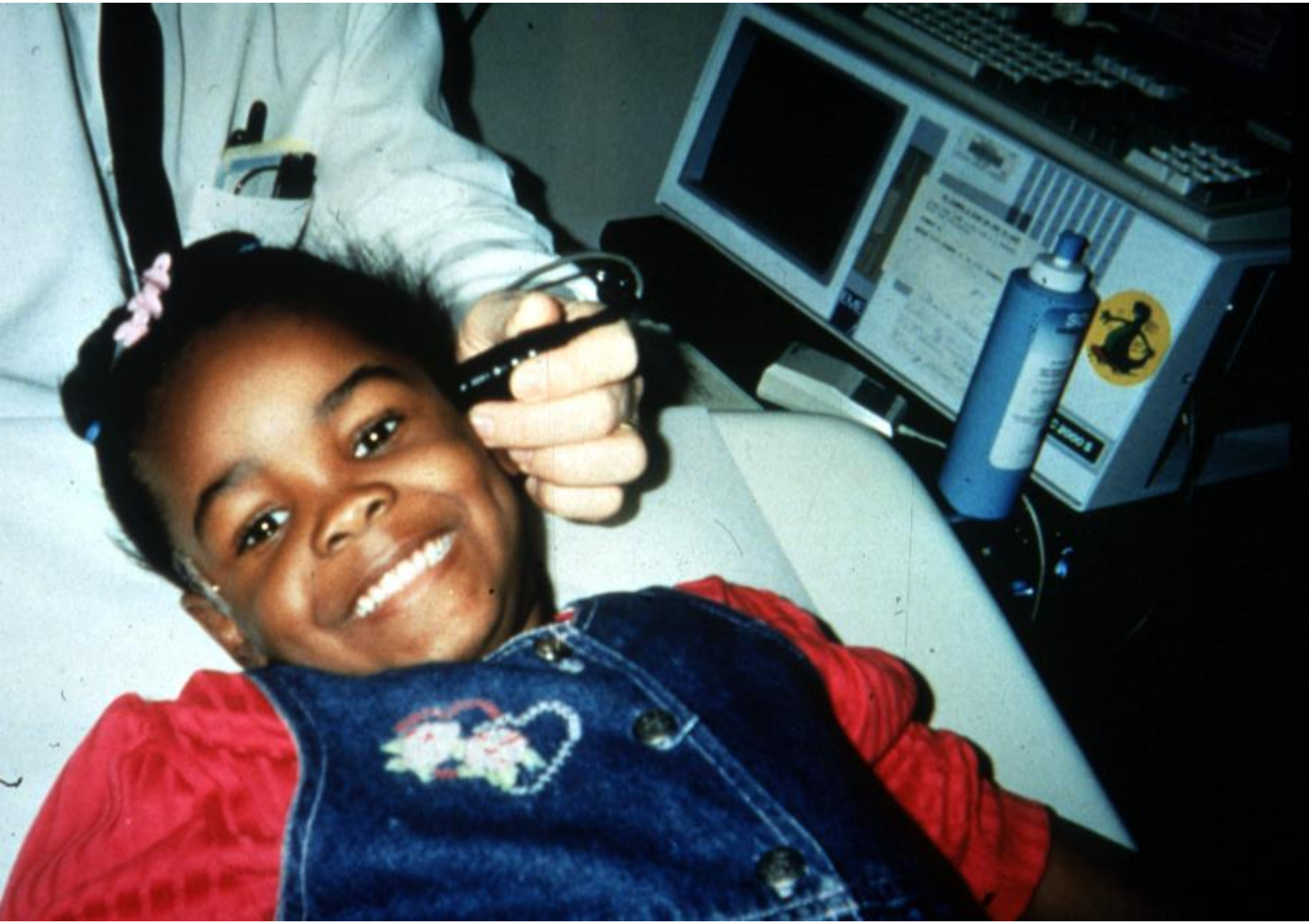
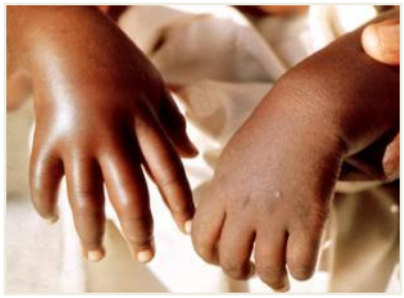
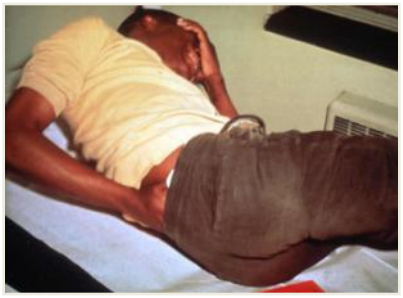
ROFSED = Réseau Ouest Francilien de Soins des Enfants Drépanocytaires.



Treatment of complications

- **PAIN**





- Infections
- Acute anaemia: ASS, aplastic crisis
- Severe vaso-occlusive events: ACS, strokes, priapism, organ failure
- Pulmonary hypertension
- Complications in high-risk pregnancies

Transfusion therapy is a cornerstone for management of SCD complications

Screening neonatale?

PROGRAMMA DI SCREENING NEONATALE

- Scopo: eliminare o ridurre mortalità, morbidità e “disabilities” che sono il risultato della malattia inclusa nel pannello di screening.

- Scopo screening emoglobinopatie :”diagnosi presintomatica e trattamento precoce della anemia falciforme ”.

- Opportunità di counseling genetico alle famiglie

Kladny B1, Williams A, Gupta A, Gettig EA, Krishnamurti L.
Genetic counseling following the detection of hemoglobinopathy trait on the newborn screen is well received, improves knowledge, and relieves anxiety. Genetics Med.2011.13.7:658-661

COMPREHENSIVE CARE PROGRAMME

Newborn Screening for Sickle Cell Disease: Effect on Mortality. Vichinsky E et al. Pediatrics 1988; 81:749

PEDIATRICS
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

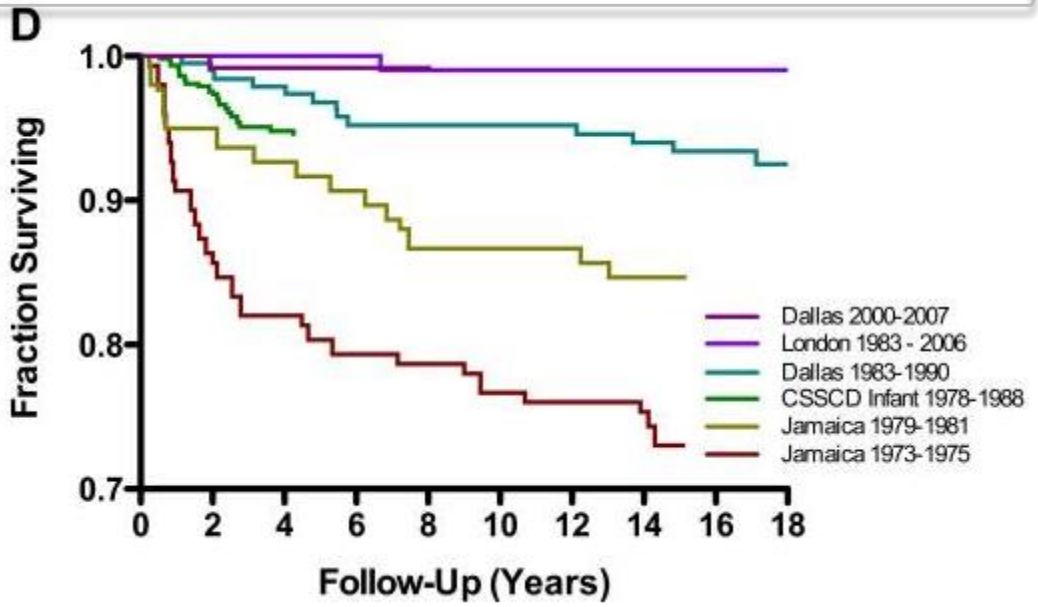
Lo studio ha dimostrato

Mortalità: - 1,8% se Dx alla nascita
- 8% se Dx > 3 mesi di vita

→

- Dx neonatale
- Profilassi penicillinica < 3 mesi di vita
- Informazione delle famiglie
- Follow-up periodici

Lo studio condotto da Quinn *(Quinn et al. Blood 2010)* su bambini entrati a far parte di un programma di screening neonatale condotto tra il 1983 e il 2007 ha dimostrato una sopravvivenza a diciotto anni del 94%



Diversi programmi di screening neonatale

LINEA GUIDA GRAVIDANZA FISIOLOGICA
Aggiornamento 2011 (106-108)

- Emoglobinopatie

Quesito 33 :

Lo screening delle emoglobinopatie dovrebbe essere offerto a tutte le donne in gravidanza oppure solo alle donne a rischio?

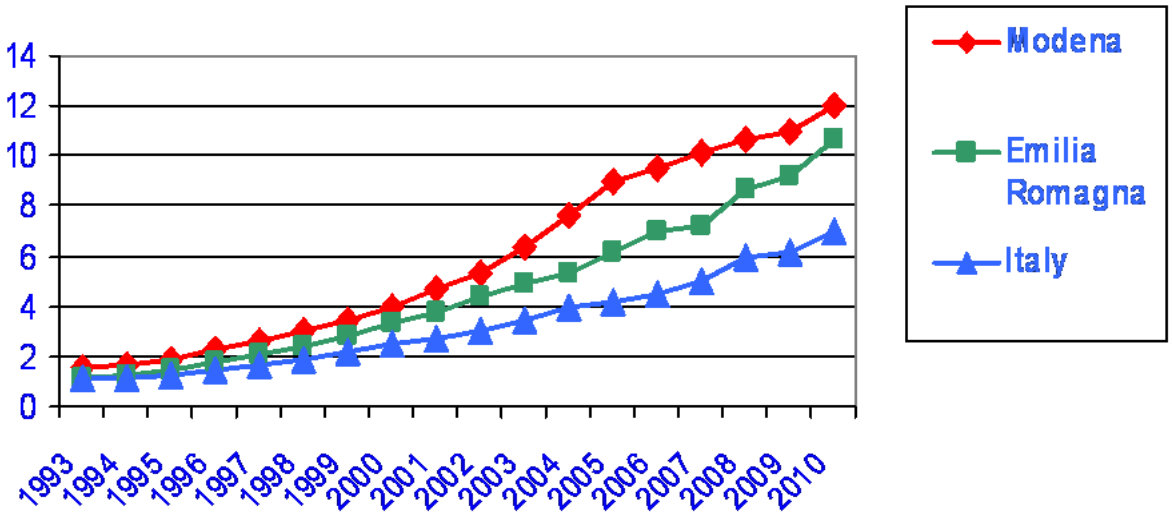
LINEA GUIDA

Sistema nazionale per le linee guida

Gravidanza fisiologica

AGGIORNAMENTO 2011

FENOMENO MIGRATORIO

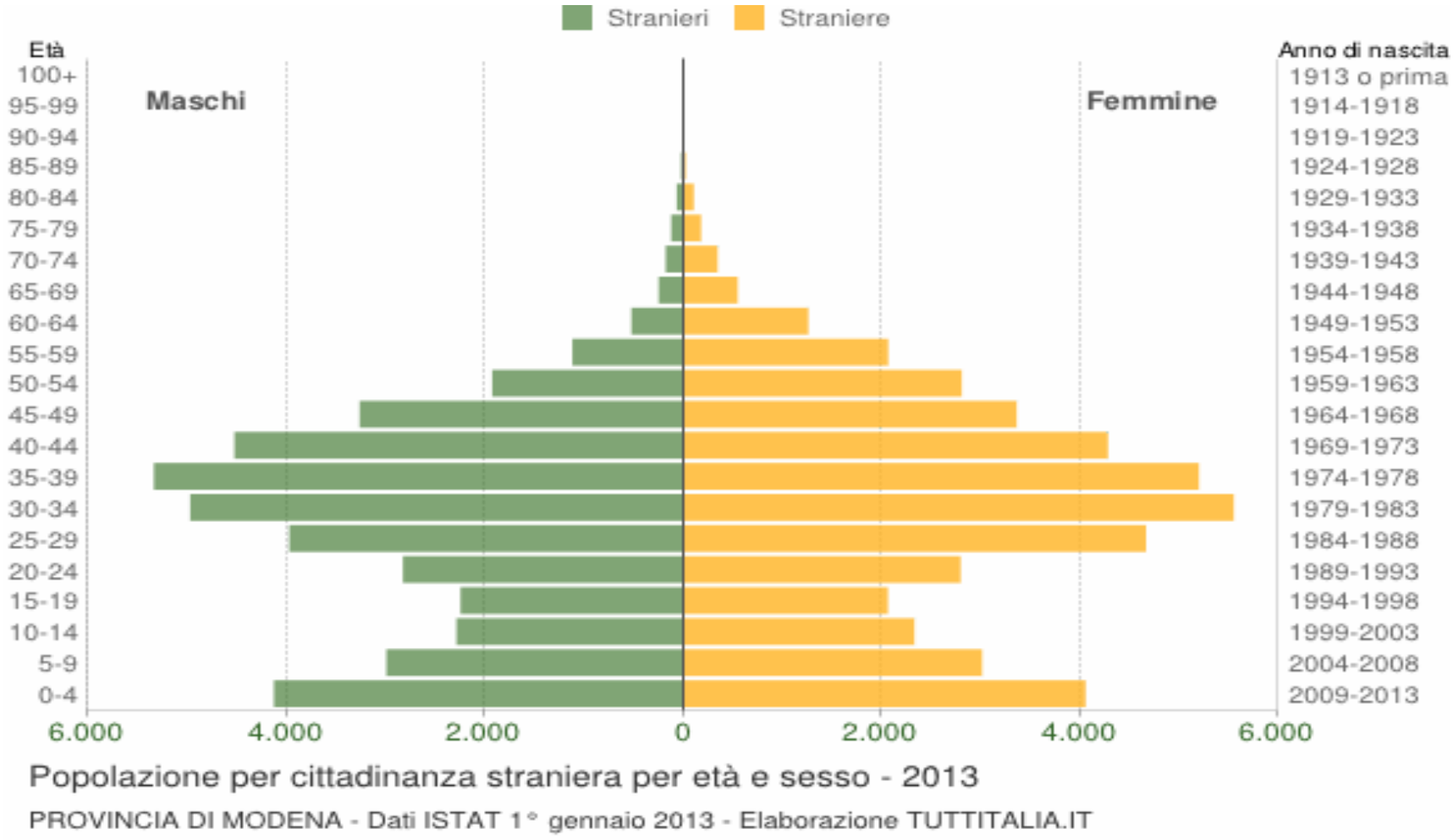


Italia: 4.36 x 10^6 di immigrati (**6,8 % popolazione**), particolarmente concentrate nelle Regioni Settentrionali (ISTAT) la maggior parte dei cittadini stranieri si concentra nel Nord (35,2% nel Nord-ovest, 26,6% nel Nord-est) e, in misura inferiore, nel Centro (24,2%) A livello regionale le differenze si manifestano in modo ancora più evidente. L'incidenza assume valore massimo in Emilia-Romagna, dove la popolazione straniera rappresenta l'11,2% del totale dei residenti, in Lombardia (10,5%) e Veneto (10%)

Emilia Romagna: 154.317 immigrati da aree endemiche, di cui il 55% nell'aerea Nord (Parma, Piacenza, Modena, Reggio Emilia) (ISTAT)

Courtesy D:Venturelli 2015

IMMIGRATI NELLA PROVINCIA DI MODENA



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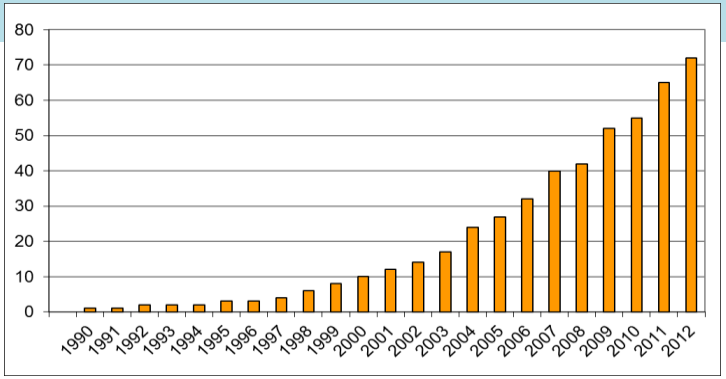
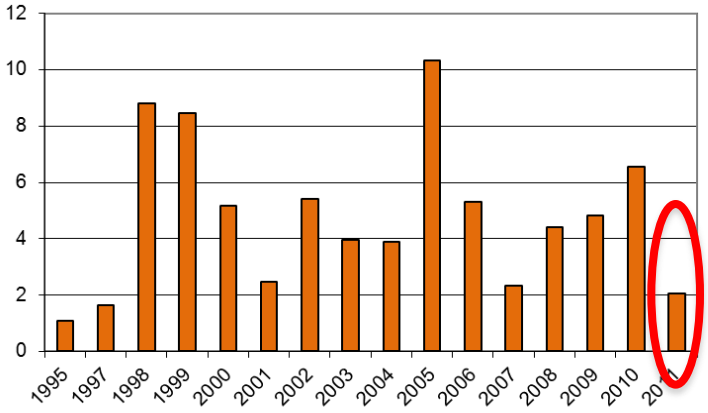
PROGRAMMA DI SCREENING NELLA PROVINCIA DI MODENA

BACKGROUND

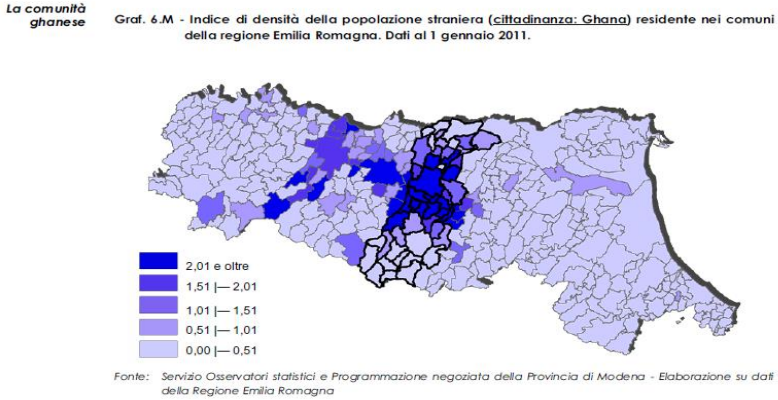
Incremento di nuove diagnosi in età pediatrica





Inizio della profilassi con penicillina non nei tempi previsti

Costante aumento di nuovi nati da madri provenienti da aree endemiche (fenomeno migratorio)



Legge 219/95.art.5,comma 1°,punto 9 (prevenzione di problemi immunoematologici e MEN)

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RACCOMANDAZIONI

- In epoca preconcezionale, a tutte le donne devono essere assicurati counselling e test in grado di identificare le portatrici di emoglobinopatie (anemia falciforme e talassemia).

Giunta della Regione Emilia Romagna. Delibera 1097/2011: ***"Indicazioni alle aziende sanitarie per la presa in carico della gravidanza a basso rischio in regime di DSA2 a gestione dell'ostetrica"***.
Cod.GPG/2011/1234 2011:15

→ *Queste raccomandazioni attribuiscono valore di favorevole rapporto benefici/danni e benefici/costi dello screening universale in aree con elevata prevalenza di emoglobinopatie, come quella del bacino del Mediterraneo*

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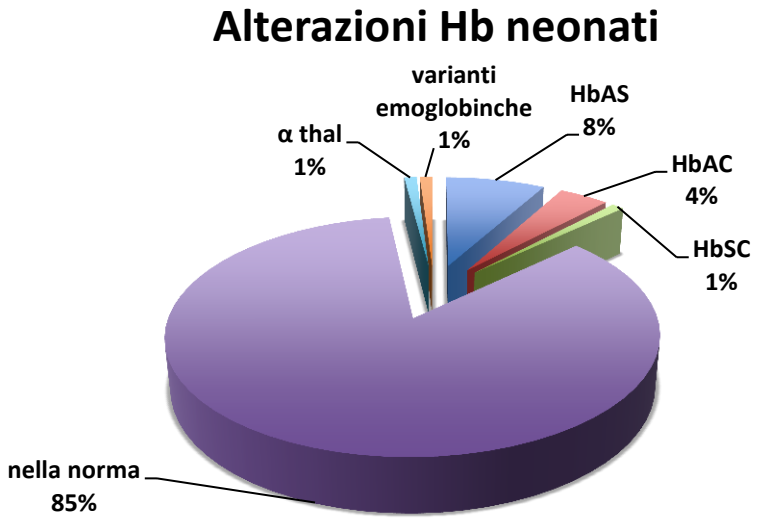
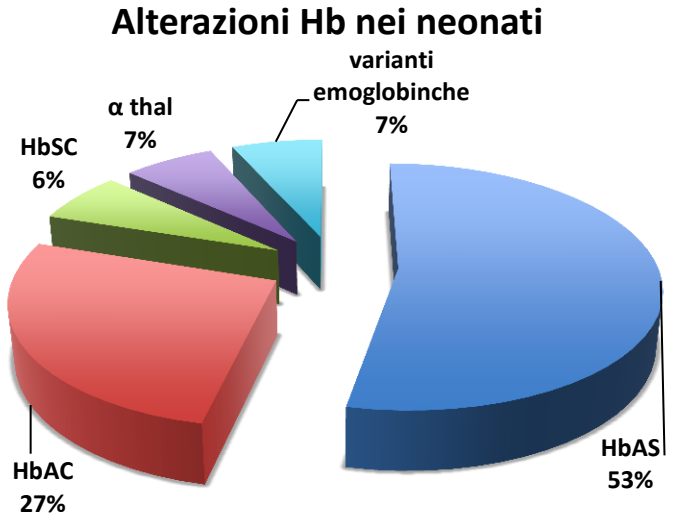
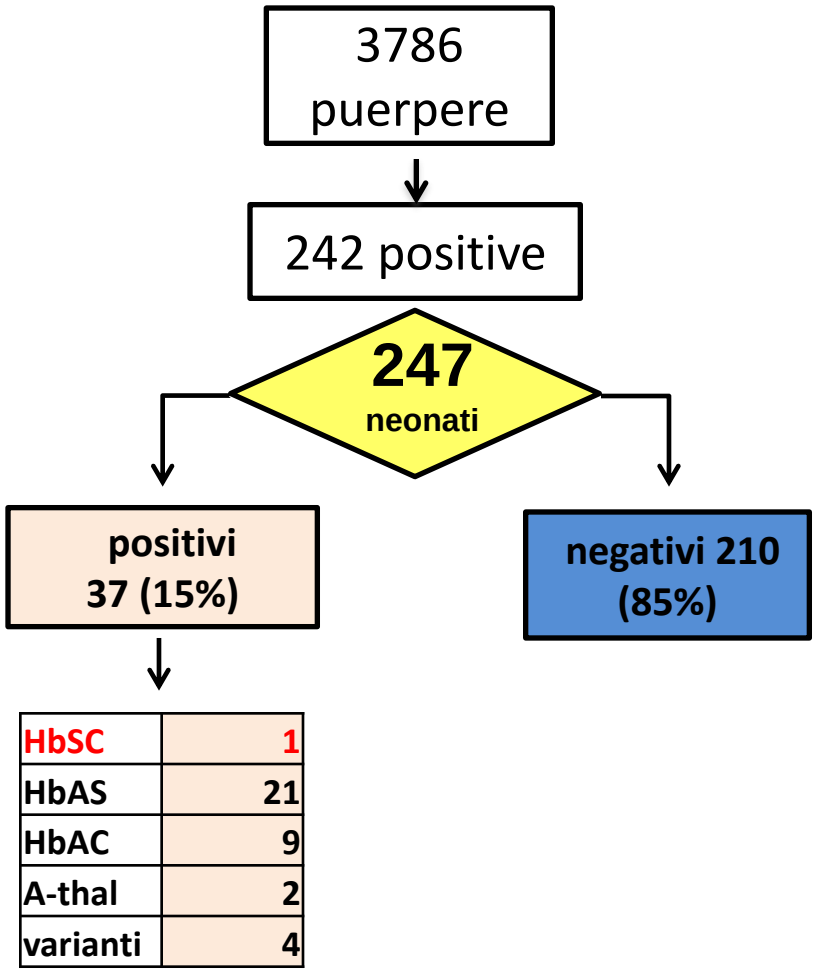
VARIANTI EMOGLOBINICHE dei NEONATI delle puerpere positive







HbSC	1
HbAS	21
HbAC	9
A-thal	2
varianti	4

L'incidenza di anomalie emoglobiniche sulla popolazione totale delle gravide fino ad ora analizzate, risulta essere di circa il 6% DIAGNOSI 5.6 GIORNI

CONSULENZA E PRESA IN CARICO U.O.ONCOEMATOLOGIA PEDIATRICA

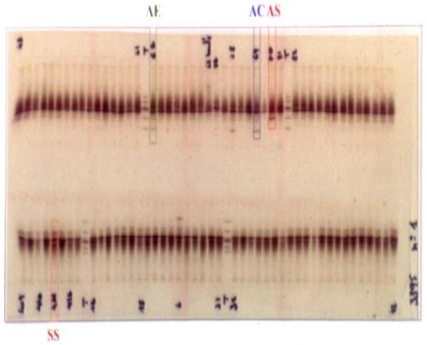
10 neonati identificati (4HbSS-6HbSC)

- Appena Possibile (entro 1 mese):

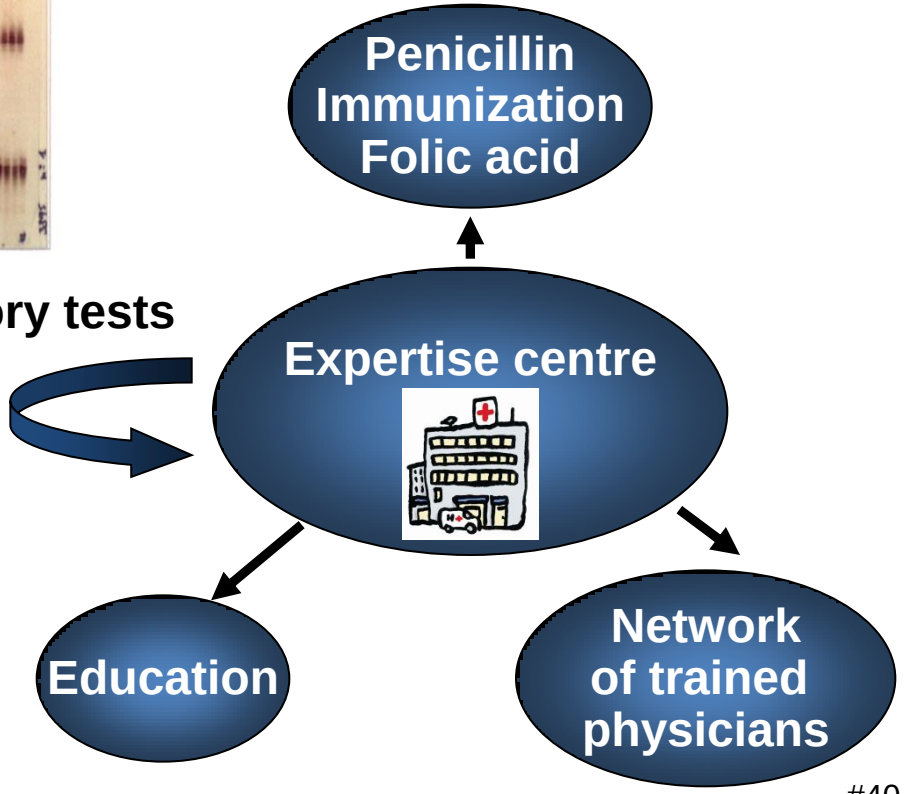
  – Conferma diagnosi (nuovo prelievo-sangue periferico/DNA/SMT)
  – Colloquio informativo introduzione alla malattia e inserimento
    lista malattie rare Regione Emilia Romagna
  – Informazione somministrazione profilassi antibiotica vaccinazioni e gestione episodi febbrili
  – Test fratelli
  – Comunicazione pediatra di base

Neonatal screening

IEF



Confirmatory tests



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