Thalassaemia control

the example of Cyprus

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The Case of Cyprus

Situated in the eastern Mediterranean

- **Area 9,250 km^2**
- **1,138,071 inhabitants (2012)**

History of the Control of Thalassaemia in Cyprus

- First concise report by Dr A Fawdry – medical officer at Cyprus MoH
  - ➔ 1944 – Lancet
  - ➔ 1946 – Transactions of the Royal Society of Tropical Medicine and Hygiene

- Early 1960s - Thalassaemia recognised as a major public health problem
- At the time, limited knowledge of the pathology, clinical outcome, diagnosis and prevention
- 1971 – the Cyprus government sought support from WHO (G. Stamatoyiannopoulos, Univ. of Seattle, WHO consultant)
- 1972 – Establishment of a 5-year national plan based on WHO recommendations

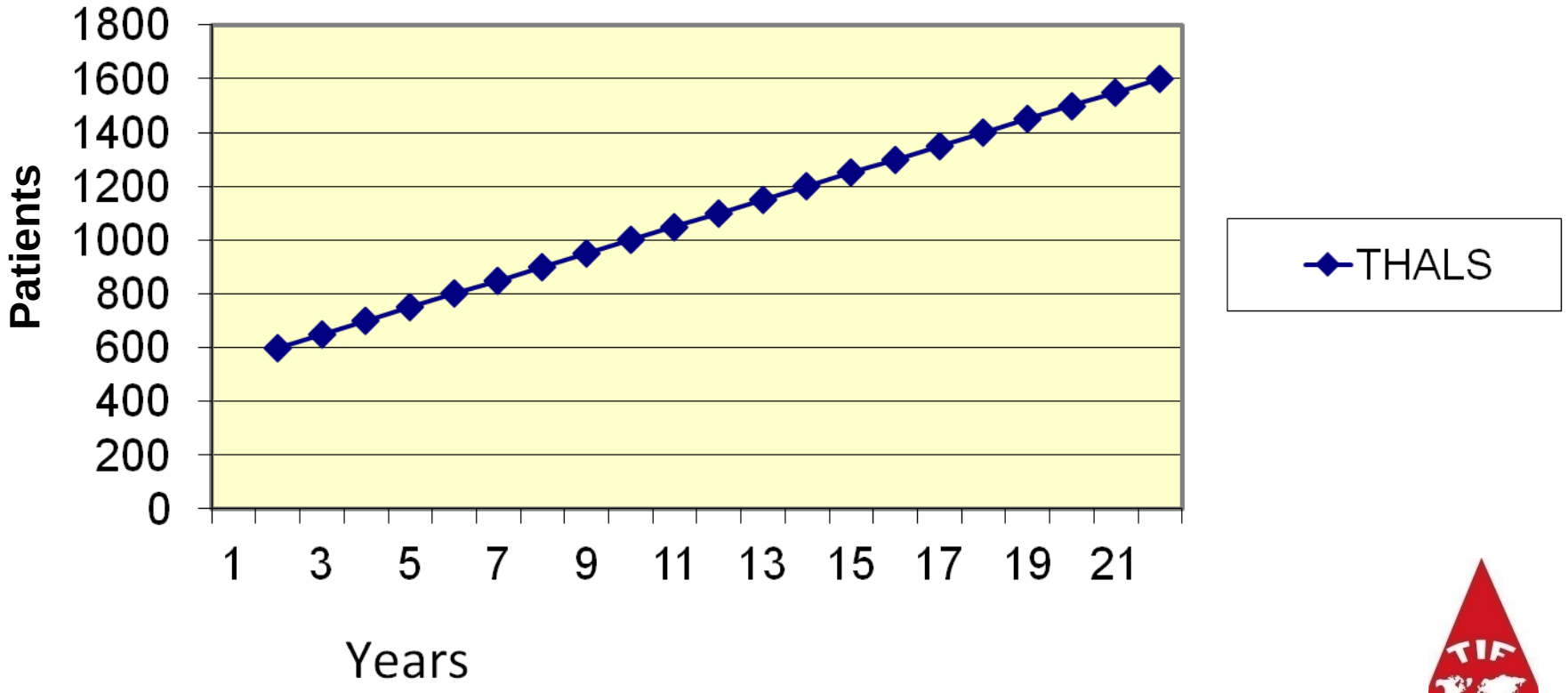
WHO recommended establishment of a national control programme (1972)

- ➔ **Effective prevention or limitation of new affected births**
- ➔ **Resources to be freed and spent on providing appropriate healthcare to living patients**

A major concern was to provide holistic support to then known living patients with β-thalassaemia major

Accumulation of cases

Assuming full survival and no prevention



WHO estimated in 1971 that in the absence of effective prevention by 2010…

- ➔ **Increased survival could lead to a rise in prevalence from 1:1000 to 1:138, which could result in an increase of**
- ➔ **cost of treatment of 600–700%**
- ➔ **Prevention costs/1 year = treatment of existing patients (500) for 8 weeks**
- ➔ **the blood requirements of 300–400%**

More than 50% of the population would have to become blood donors

Epidemiological studies confirmed occurrence across the island

- 1:7 (14%) Cypriots is a β-thalassaemia carrier
- 1:49 (2%) couples at risk for β-thalassaemia major (both partners heterozygous)
- 1:192 newborns annually expected to be homozygous (60-70 babies) or 5.5/1000 livebirths
- 1:1000 (0.1%) prevalence of homozygotes in the population
- 1:5 (20%) carry α-thalassaemia genes
- 1:500 (0.2%) carry sickle cell gene

Prevention strategies

- Public education and awareness
- Population screening. Specialised labs
- Genetic counselling. Counsellors?
- Prenatal diagnosis
- Pre-implantation diagnosis
- Ethical principles: voluntary, autonomy of couples, right to full information, confidentiality: informed choice

Planning Prevention Services.

- National advisory committee
- International support (WHO, TIF and others)
- Budgetary allocation.
- Monitoring and evaluation.
- Ethical control of practices.
- PHC contribution.
- NGO contribution – consultation with stake-holders, associations, medical societies .

Control Programme from 1974 Prevention & Clinical Management

A. Prevention

1972	Health education & population screening
1977	Prenatal diagnosis
1978	First diagnostic laboratory established as part of Haematology Laboratory at Hospital
1982	Thalassaemia Centre established – a special independent laboratory for population screening and genetic counselling
	and a day care centre for patients
1981	Prenatal methods established in Cyprus
1983	Introduction of "premarital certificate" by the church
1990	Molecular (DNA) methods for prenatal and other diagnoses
1998	Introduction of new technologies – pre-implantation

B. Clinical management

1965 Blood transfusion recognised as the basic treatment

1969 Desferrioxamine provided IM.

1973 A division established within Paediatric Dept of Nicosia General Hospital devoted to treatment of thalassaemia patients

1974 Establishment of first patients/parents support group

1976 Establishment of Voluntary Blood Donation Association

1982 Thalassaemia Centre opens in Nicosia (clinic and lab)

1981-2007 – Clinical management improves with development of holistic multidisciplinary care approaches

1986 Establishment of first International patients' organisation (TIF)

Angastiniotis M, Kyriakidou S, Hadjiminas M. How thalassaemia was controlled in Cyprus. World Health Forum. 1986 7:291-7

Angastiniotis M, Kyriakidou S, Hadjiminas M. The Cyprus Thalassaemia Control Program Births Defects Orig Artic Ser 1988; 23 (5B): 417-32

Components of Effective Patient care:

- **National registers**
- **Free medical treatment**
- **Expert reference centres – quality of care**
- **Voluntary non-remunerated blood donation for safe and adequate blood**
- **Psychosocial support**

Factors Contributing to Effective Control

1. Health education / awareness campaign

Active participation and partnership of:

- **Government - Ministry of Health, Finance, Education**
- **Health professionals**
- **Greek Orthodox church**
- **Patients/parents' support groups**
- **Community**
- **Mass media**

2. Campaign focused on reaching everyone

- **General public**
- **Health professionals – paediatrics, gynaecologists**
- **Policy makers**
- **Students**
- **Patients and their parents**

3. Population screening

Ideally voluntary, premarital and pre conceptual.

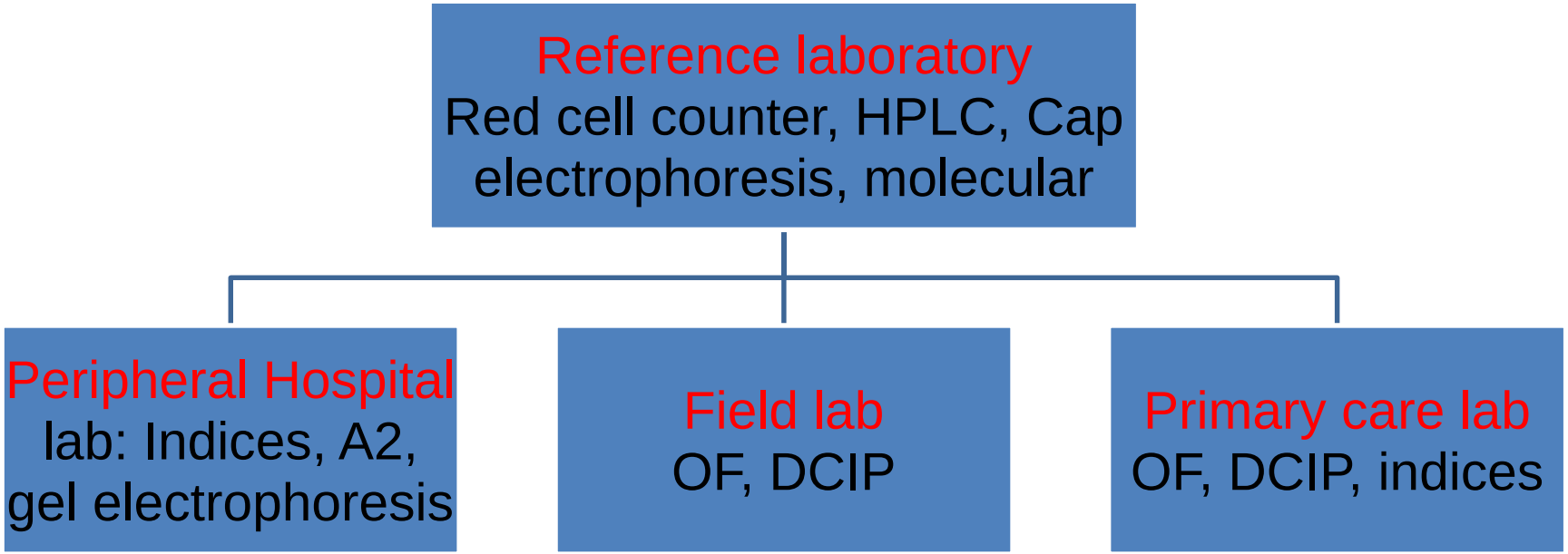
Decisions needed early on:

- **When best to screen**
- **Who to screen**
- **Who does the screening**
- **Which technique, methodology, algorithms to include**
- **Where to train laboratory scientists**

When to screen:

- **Before / after marriage**
- **When pregnant – in antenatal clinics**
- **After the birth of an affected child**
- **When a child is diagnosed in the extended family**

Laboratories for Screening



5. Genetic counselling to assist informed choices

- **Education of specialists to deliver accurate information at all levels while respecting the rights to**
  - ➔ **Full and transparent information**
  - ➔ **Confidentiality**
  - ➔ **Autonomy of the couple – choices on all aspects of prevention, diagnosis, treatment**

Non-directive, voluntary, equal access to all

Screening Phases

1972–1976

i. Married couples

ii. Engaged couples

iii. Relatives of β-thalassaemia homozygotes

iv. Final-year high school students

1976–until today

i. Pregnant women since PND became available

ii. Couples before engagement and marriage

iii. Students

1980–1989 results v. 1998 results:

diagnosed as carriers would it stop you:	1980-1989 "yes"	1998 "yes"
(a) from marrying?	10%	<1%
(b) from having your own children?	20%	<1%
Would you:		
(a) undergo prenatal diagnosis?	60%	99%
(b) proceed with pregnancy without prenatal diagnosis?	10%	2%
(c) have a termination in case of positive diagnosis?	85%	98%
(d) continue pregnancy despite positive diagnosis?	5%	2%

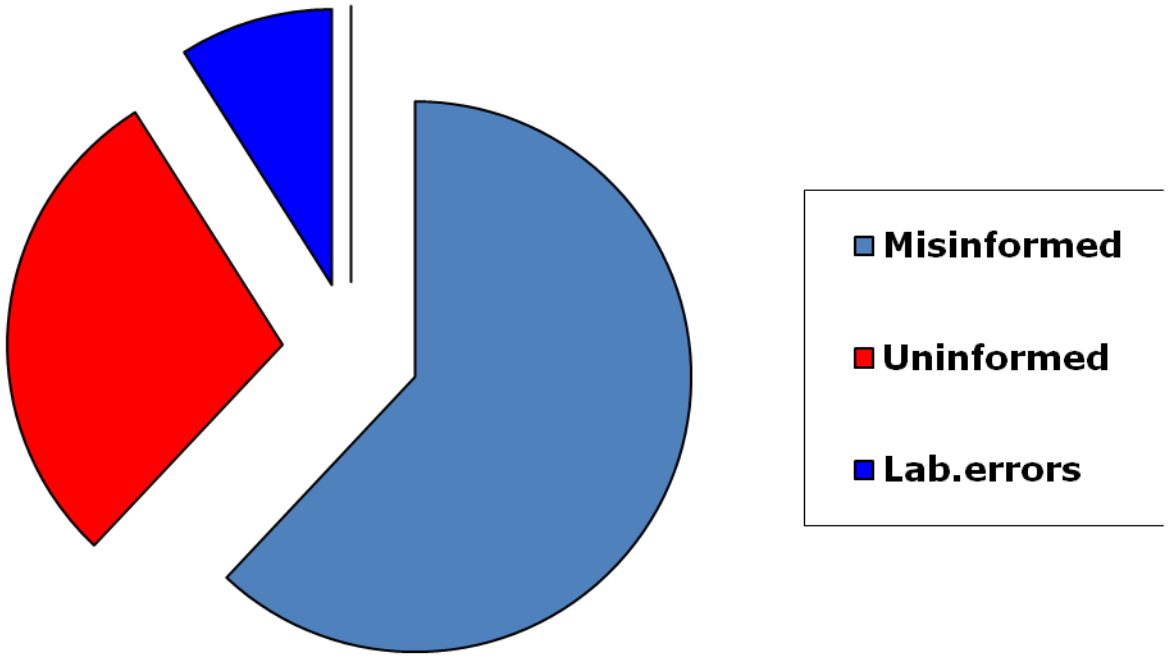
Outcome of population screening

Method	Year	Births	Expected affected births	Actual affected births	Difference	%
Introductin of genetic counselling	1976	8594	54	53	1	1.8
	1975	8039	51	48	3	6.0
	1876	9259	59	37	22	37.0
Introduction of prenatal diagnosis (outside Cyprus)	1977	9188	58	37	21	38.0
	1978	9188	61	27	34	56.0
	1979	16372	66	25	41	62.0
	1980	11087	70	20	50	71.0
	1981	10780	68	10	58	85.0
Introduction of prenatal diagnosis in Cyprus	1982	11578	73	8	65	89.0
	1983	10900	69	8	61	88.0
Introduction of premarital certificate	1984	11200	71	4	67	94.0
	1985	10421	66	2	64	97.0
	1986	10691	68	1	67	98.5
	1987	10337	65	2	63	97.0
	1988	10752	68	0	68	100.0
	1989	19372	66	0	66	100.0

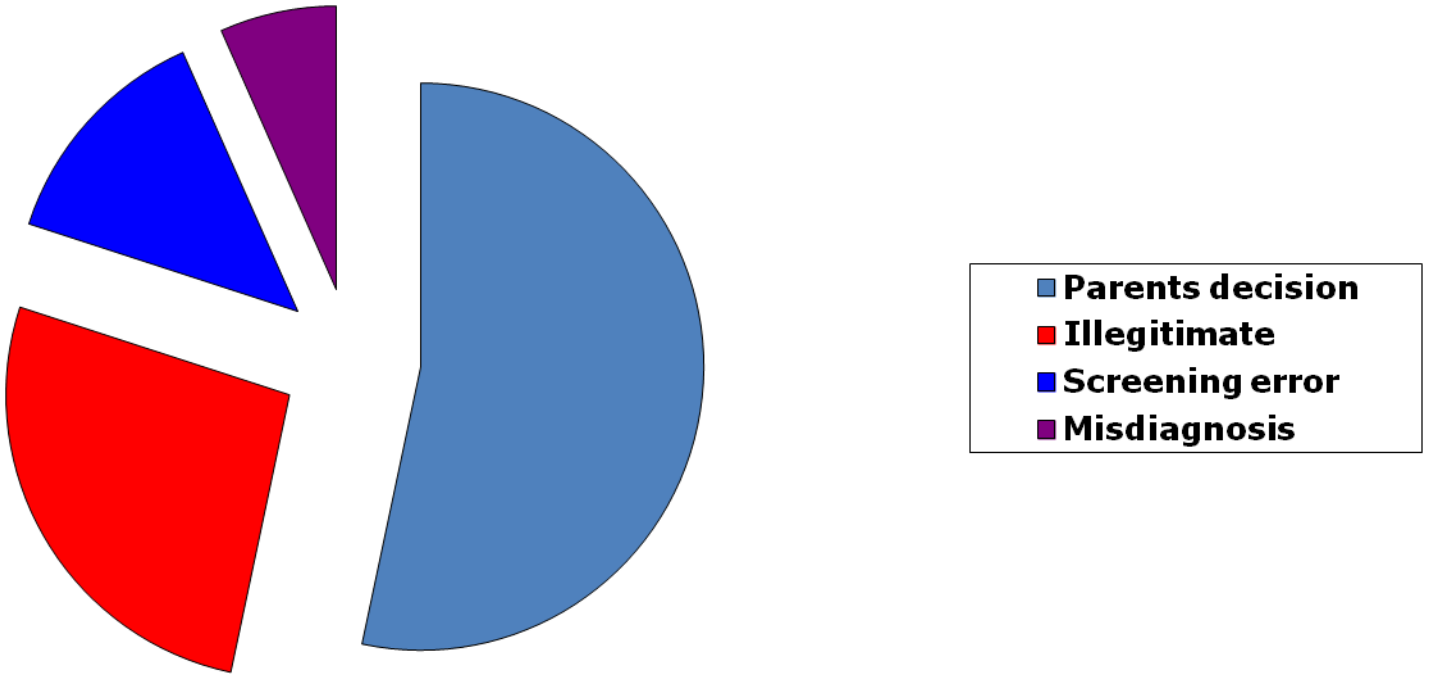
Thalassaemia genetic counselling

- Discuss the results of screening
- To know and understand their risk
- To assist them to make informed choices without being directive
- Discussion of options in a non-directive manner
- Respecting the autonomy of the couple
- This is the job of a specialist who knows thalassaemia

Residual Births Cyprus – 1978-1980



Residual Births Cyprus – 1985-94



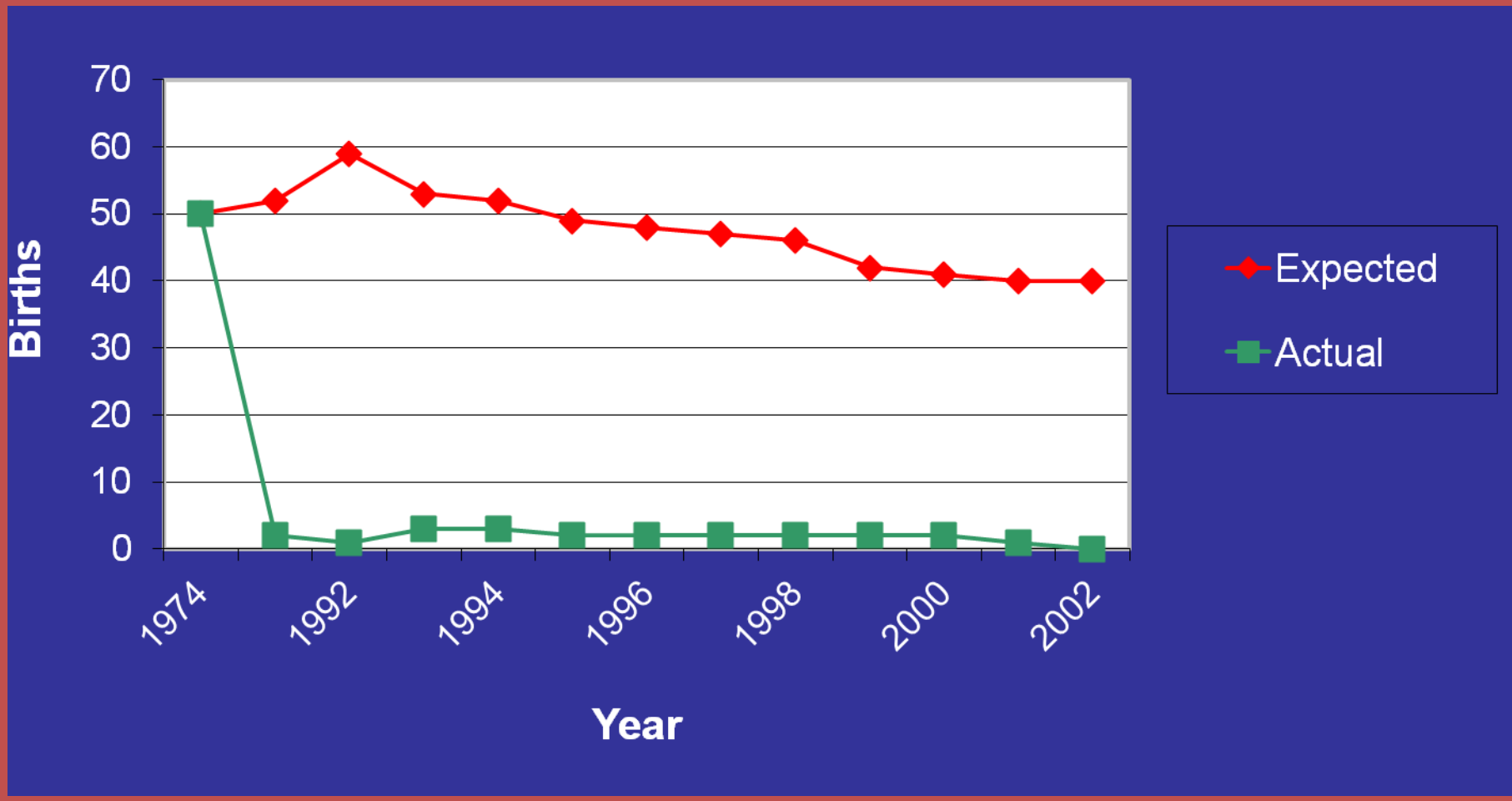
Factors contributing to its Success

- **Involvement of the church ("premarital certificate") – homogeneity in religion**
- **Small relatively homogeneous population (language, culture)**
- **High literacy rate**
- **Engagement of the public, medical community and patients/parents**
- **Strong national support associations**
- **Satisfactory health infrastructure and services**
- **Establishment of active collaboration with WHO and international experts**

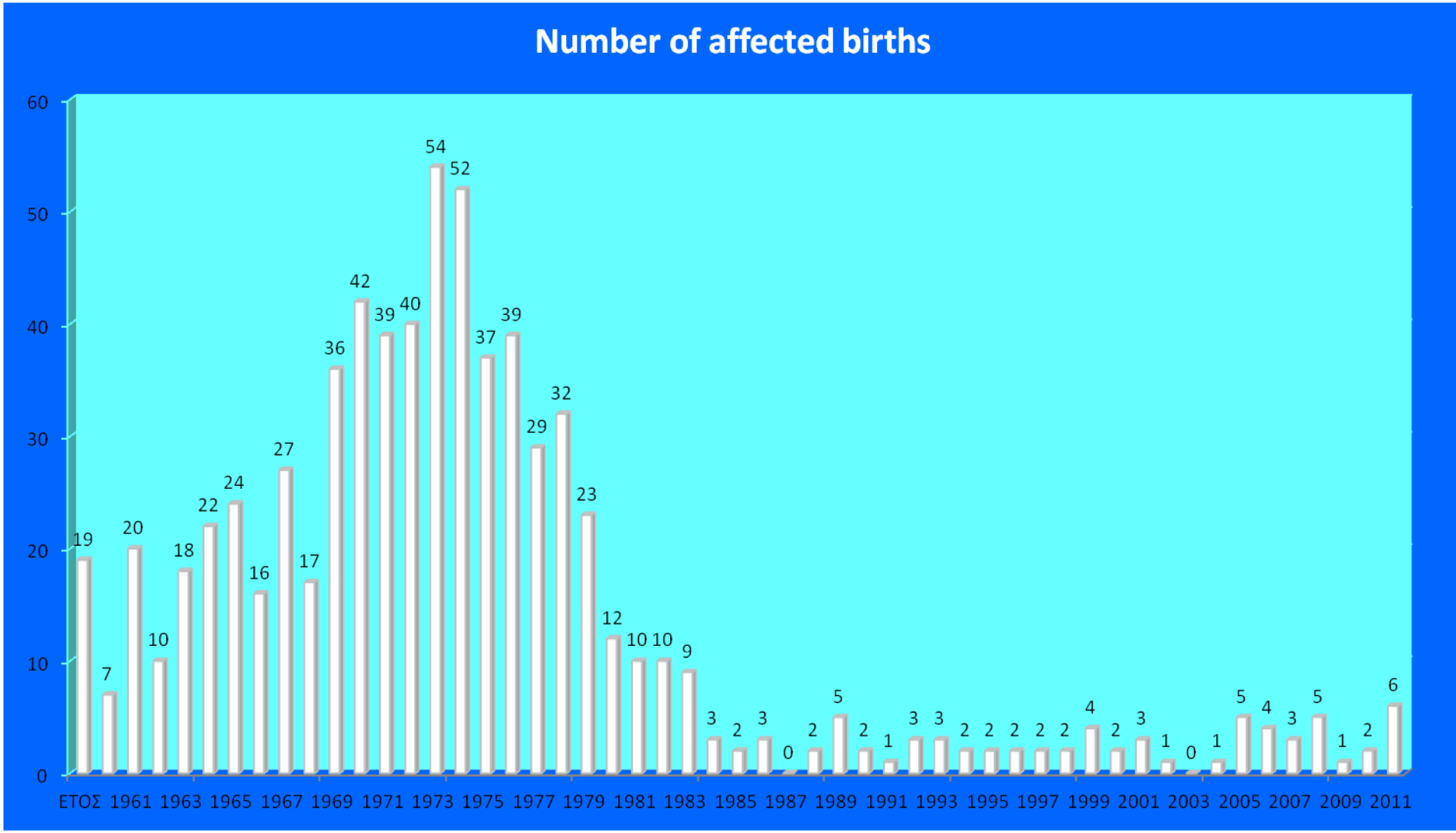
Results

The Cyprus Thalassaemia Programme

Actual vs expected thalassaemia births in Cyprus

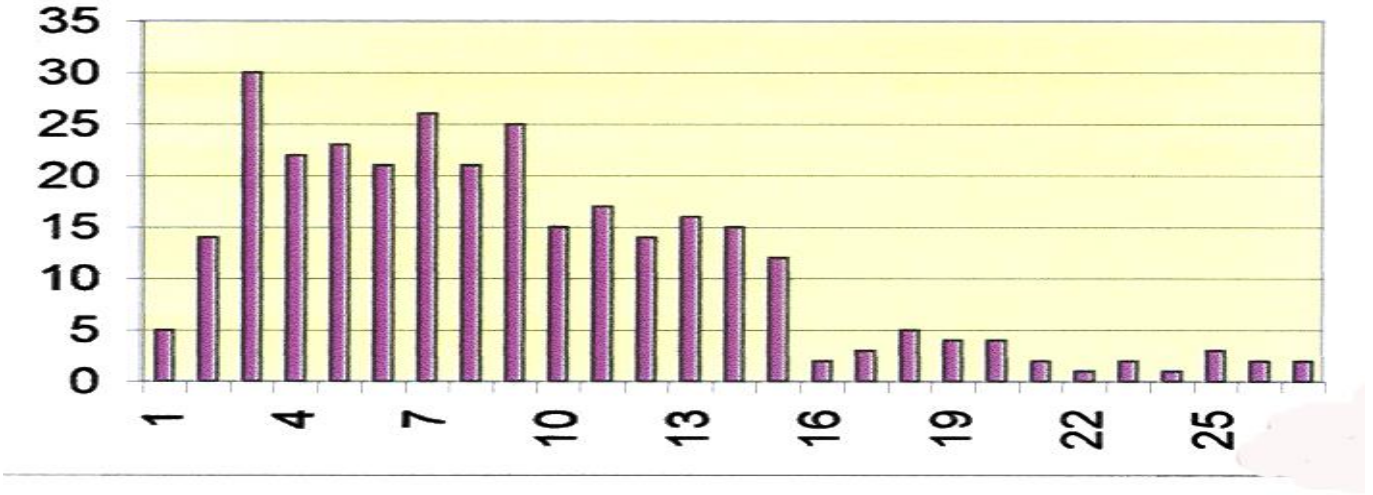


Thalassaemia patients in Cyprus by year of birth

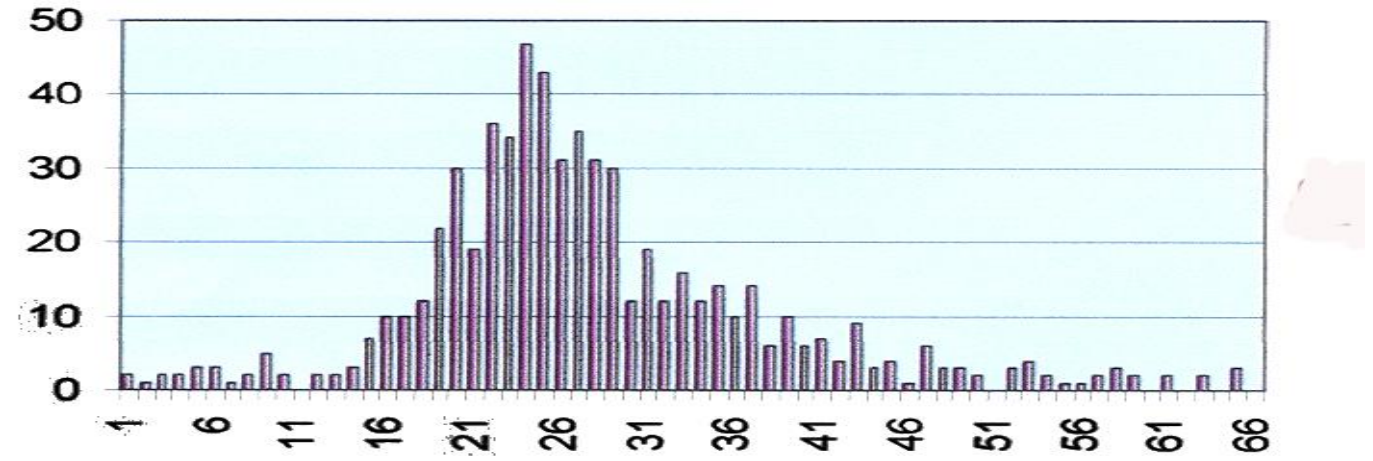


Age distribution of thalassaemia patients

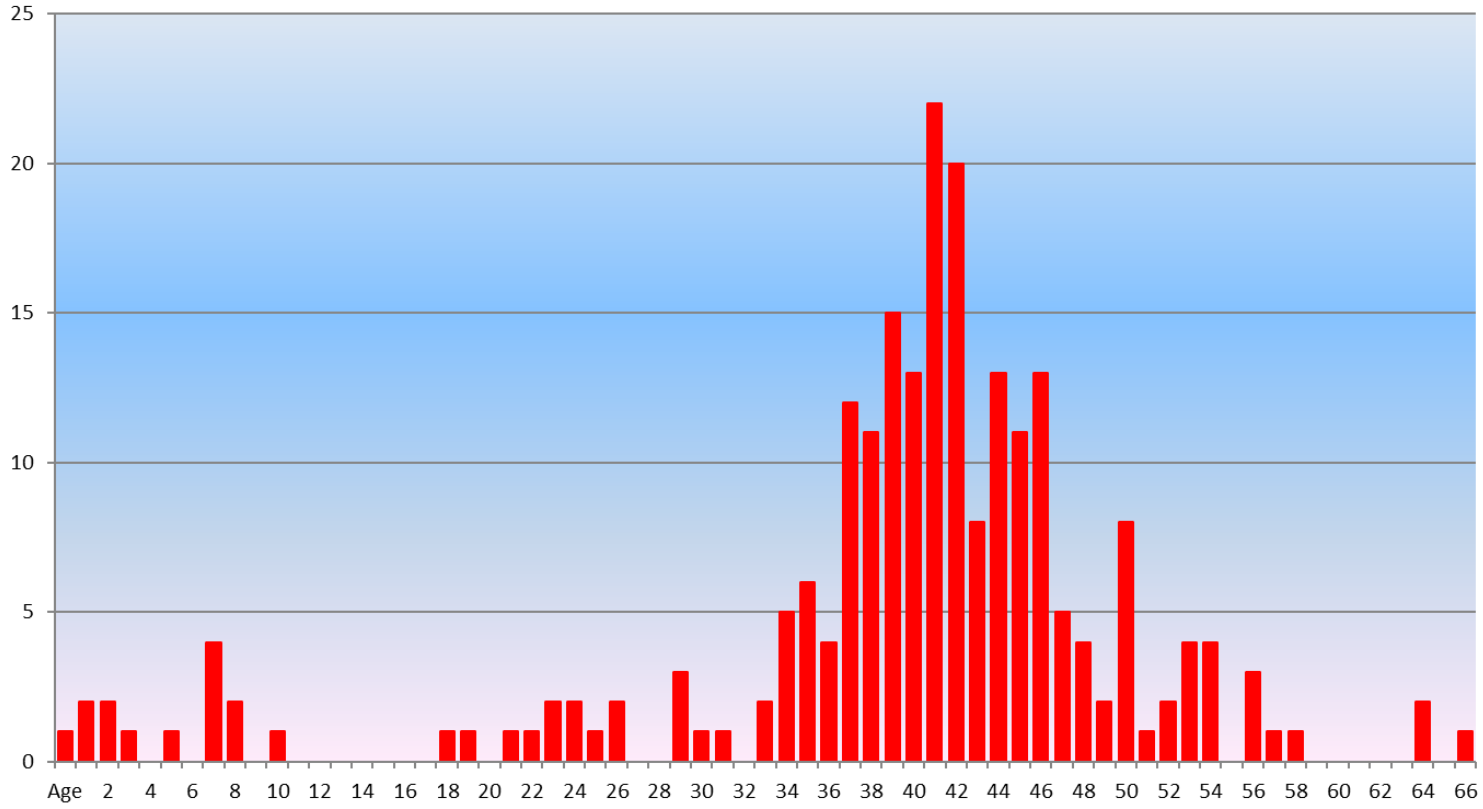
Country with no programme



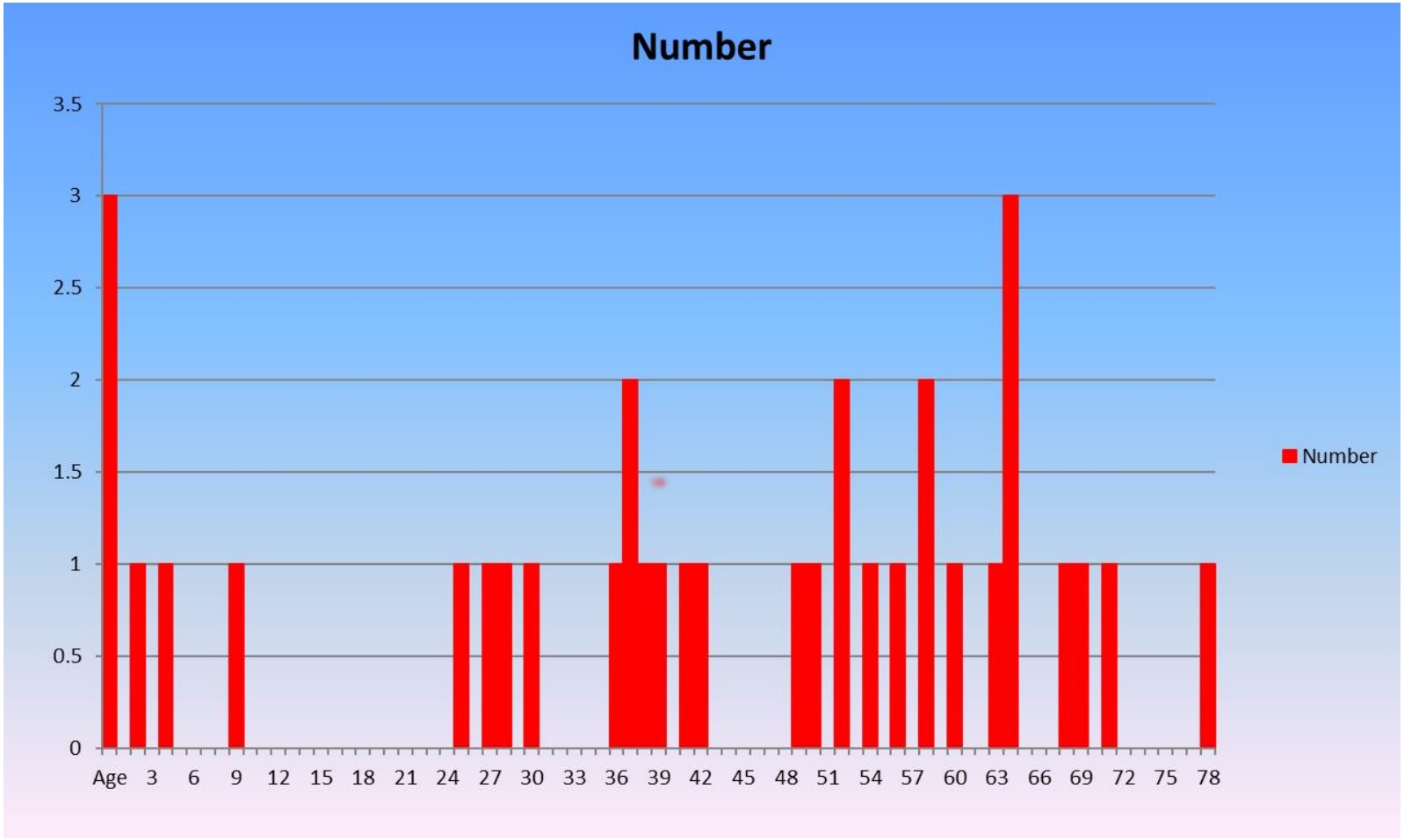
Cyprus in 1999



Age distribution of thalassaemia patients in Cyprus today



Age distribution of NTDT patients in Cyprus today



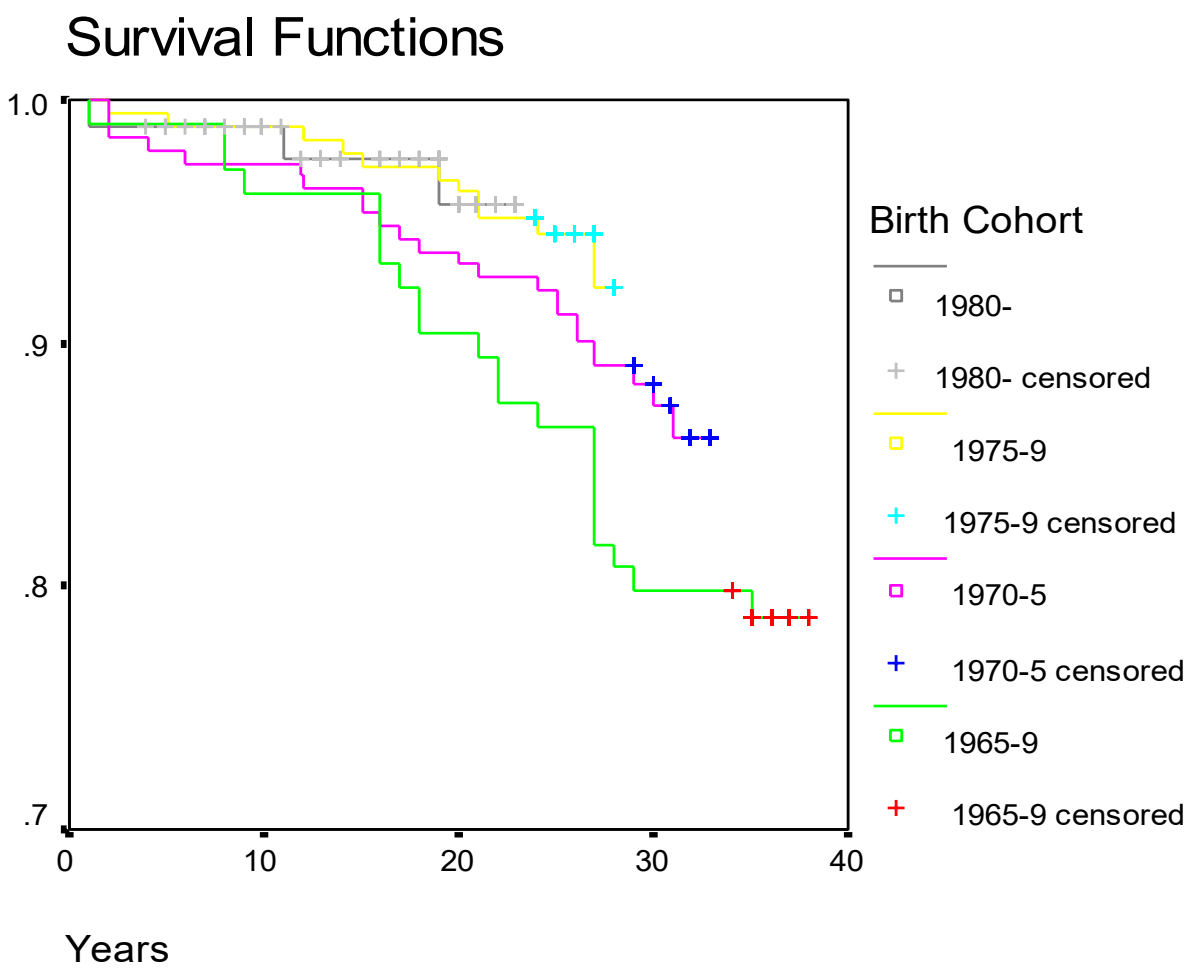
Main complications in Thalassaemics in Cyprus (all patients=647)

	No of patients (m/f)	% of patients
Hypothyroidism	84 (37/47)	13.0
Hypoparathyroidism	8 (6/2)	1.2
Hypogonadism	184 (88/96)	28.4
Diabetes	95 (51/44)	14.7
Heart failure/arrhythmias	57 (38/19)	8.8
Osteoporosis	218 (119/99)	33.7
Chronic hepatitis C	18 (10/6)	2.8
Chronic hepatitis B	5 (4/1)	0.8
Cirrhosis	10 (8/2)	1.5

Thalassaemic Population in Cyprus

- **Total number of patients with thalassaemia syndrome: 928**
- **β-thalassaemia: 694 out of which**
  - **β-thalassaemia major: 592**
  - **β-thalassaemia intermedia: 102**
- **α-thalassaemia: 179**
- **Sickle cell anaemia: 39**

Cyprus thalassaemics: overall survival



Conclusion

- **Prevention benefits the patients by saving resources for their treatment.**
- **Early (before marriage) identification of carriers gives young couples the most choices.**
- **The health services can offer quality care so patients have quality of life as well as survival.**

Nicosia Thalassaemia Centre

Change in Care

Change in Outcome