

Provision of Clinical Management services in Cyprus

CONSULTATION MEETING

PREVENTION & CLINICAL MANAGEMENT OF THALASSAEMIA

25 - 26 April 2018

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Nicosia Thalassaemia Clinic



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Thalassaemia

Multifactorial Disease

Factors

- Anaemia and its treatment
- Haemosiderosis and drugs' side effects
- Age (Thalassaemics became older)
- Life Style
- Immune System



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Complications in Thalassaemia

- **Complications**

Due to:

- Anaemia → Megalocardia, Right ventricular heart failure, Pulmonary hypertension, Arrhythmias, Bone Marrow expansion, Extramedullary haematopoiesis, Osteoporosis



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Complications in Thalassaemia

(continue)

- Blood Transfusion → Viral Infections, Reactions, Allo and autoimmunization
- Haemosiderosis → Cardiac, Endocrine, Renal problems, Hepatic problems,



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Complications in Thalassaemia

(continue)

- Drugs' adverse effects → growth retardation, osteoporosis, bone disease, infections, renal and hepatic problems, ophthalmologic, auditory, arthralgia, gastrointestinal problems
- Low immune system's activity → Infections



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Comparison of chelators

Property	DFO	Deferiprone	Deferasirox/Exjade
Usual dose (mg/kg/day)	25–60	75	20–40
Route	sc, iv (8–12 hours, 5 days/week)	Oral 3 times daily	Oral Once daily
Half-life	20–30 minutes	3–4 hours	12–16 hours
Excretion	Urinary, fecal	Urinary	Fecal
Adverse effects	Local reactions, ophthalmologic, auditory, growth retardation, allergic	Gastrointestinal disturbances, agranulocytosis/ neutropenia, arthralgia	Gastrointestinal disturbances, rash, mild non-progressive creatinine increase, ophthalmologic, auditory
Status	Licensed	Licensed outside US/Canada	Approved



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Complications in Thalassaemia

(continue)

- Splenectomy → thrombosis, infections
- Hypercoagulability → thrombosis, Deep Venous Thrombosis, Pulmonary embolism, Transient ischemic attack(TIA), Recurrent arterial thrombosis



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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
Thrombosis	38	5.9

Treatment

In Cyprus all the treatment is provided free of charge, by the government of Cyprus



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Clinical Management

- Blood Transfusion
- Chelation Treatment
- Splenectomy
- Follow up protocol
- Support Therapy
- Management of Thalassaemia's complications
- Psychological Support
- B.M.T



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NicosiaThalassaemia Clinic's Staff

- Multidisciplinary Team
- The Staff is the same as long is possible, stability of the staff
- Dedicated staff, with experience in Haemoglobinopathies
- Trained in Haemoglobinopathies through meetings, seminars and conferences



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Multidisciplinary Team (MDT) Nicosia Thalassaemia Clinic Staff

- *Clinic's Medical Staff*

 - General Practitioner

 - Haematologist

 - Internist

- *Nurses*

 - 1 sister

 - 8 staff nurses

- *Secretary*

- *Nurse assistant*

- *Cleaning Lady*



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Multidisciplinary Team

- *Close Collaboration*

- Cardiologist
- Endocrinologist
- Hepatologist
- Radiologist
- Surgeon
- Haematologist
- Orthopaedic
- Gynaecologist



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Patients Transition

- Pediatrics

Few new cases , so many few children were followed in the clinics

- Adult Medicine, In the Clinic

From 2006 there are new thalassaemics' births

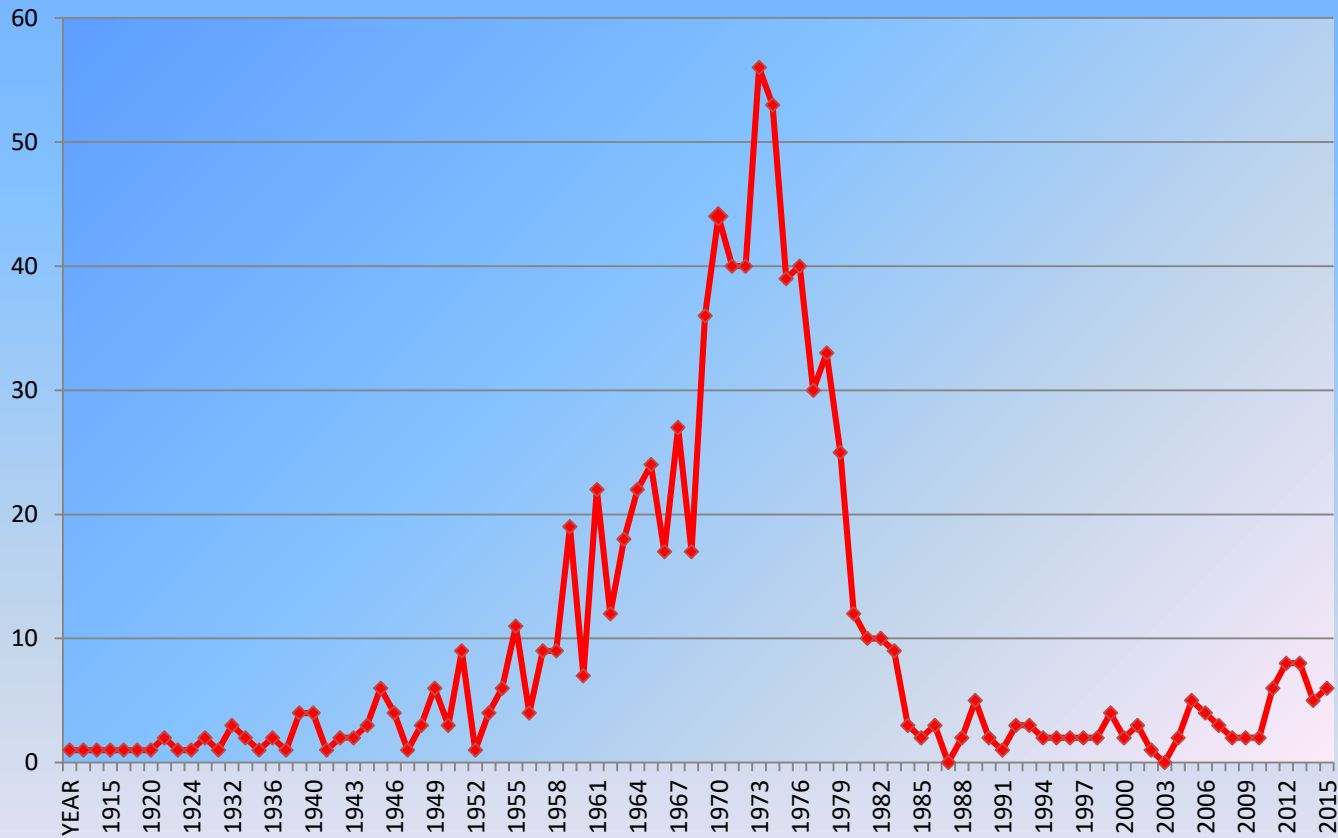
- Pediatric and Adult Medicine



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New births of Patients with Thalassaemia

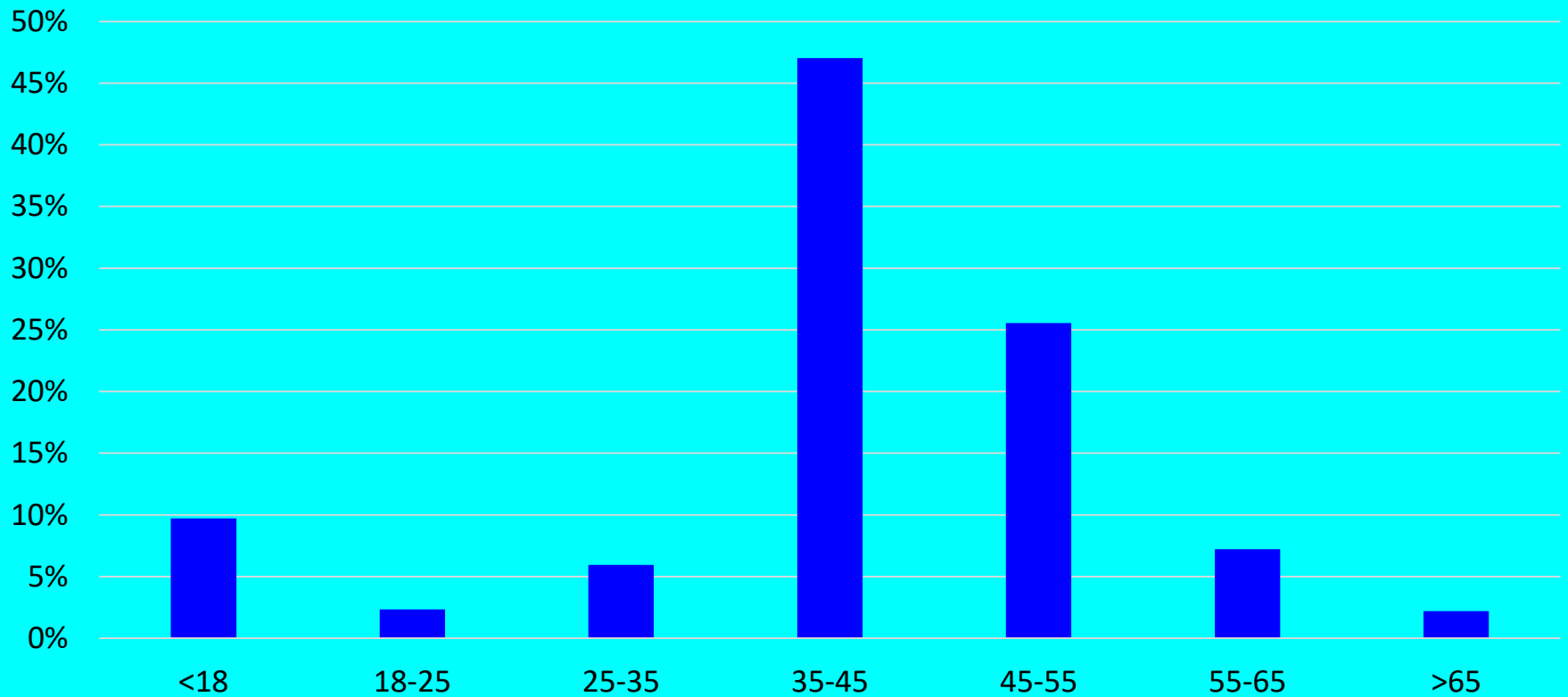


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Cyprus Thalassaemics' Age Distribution

Cyprus Thalassaemics' Age Distribution



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Pediatric Team

- *Close Collaboration*
 - Paediatrician
 - Paediatric Cardiologist
 - Paediatric Endocrinologist
 - Paediatric Gastroenterologist
 - Paediatric Nephrologists



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Paramedical specialty team

- Nurse Staff
- Psychologist
- Nutritionist
- Social Worker



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DEFERIPRONE
EVALUATION IN
PAEDIATRICS



Function of the *Thalassaemia* MDT

Stuff's Regular Meetings

A. All staff's meeting

Discussion about

-Organization issues

-Clinic's Problems

-Events' Organizations

-Patients' management

Meeting's minutes are kept



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Stuff's Regular Meetings

B. Medical Stuff's meeting

Case review , on the present of the patient , who actively participates in the discussion and all the decision are taken with his consent

- Diagnostic results
- Complications
- Investigation needed
- Treatment
- Compliant issues
- Recommendations

All the discussed issues are written in the patient's notes and all the recommendations are given in written way to the patient



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Thalassaemia Clinic's Working hours

- Day care Clinic
- Monday- Friday from 7 a.m.-7p.m.
On Wednesday from 6.30a.m. -7p.m.
- On clinic's not working hours patients are consulted in the Emergency Department or in other doctors while informed the clinic's doctor
- If patients require hospitalization are referred to the hospital to the proper specialty



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Clinic's Building

- *Dedicated* , only for patients with haemoglobinopathies
- *Not Isolated* , it is a part of the hospital and connected with it, with 2 entrances , one separate



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Patients' Clinical records

- Patient's data are kept in 2 forms
 - Written paper form
 - Electronic form, electronic patient's record



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Patient's Clinical records content

- Personal Data
- Mutation of thalassaemia
- Tests' results (blood test, radiological tests, clinical reports)

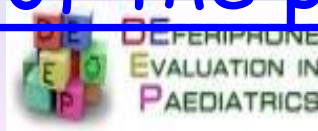


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Patients' Clinical records, Blood Transfusion data

- Blood transfusion data
 - date and levels of pre transfusion haemoglobin
 - date of blood transfusion
 - blood group and phenotype
 - amount and type of blood
 - date collection
 - number of the pint
- transfused blood



Clinical records content (continue)

- Treatment
- Splenectomy data
- Chelation data
- Pregnancies' data
- Vaccines' data



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Clinical Services at Nicosia Thalassaemia clinic

- Set Diagnosis of the disease
- Follow up protocol
- Treatment
 - blood transfusion
 - chelation
 - diagnosis and treatment of complications



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Clinical Services at Nicosia Thalassaemia clinic (continue)

- Management of Splenectomy
- Management of pregnancies with close collaboration with obstetrician
- Psychological support
- Management of B.M.T.
- Genetic Counseling to the couples at risk to have a child with haemoglobinopathy



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Diagnosis of the disease

Prevention Laboratory in Thalassaemia Center

- FBC, Microscopic examination, Hb Electrophoresis

Thalassaemia Molecular Biology Laboratory CING

- Detection of β , α , δ -thal Mutations, Xmn, Detection of abnormal Hb



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The Molecular Basis of Thalassaemia in Cyprus

β -thal 14%

IVSI nt110

IVSI nt1

IVSI nt6

IVSII nt745

C39

-87

IVSII nt1

FSC 8 (-AA)

FSC 5 (-CT)

+33

-101

+30

α -thal 20%

$-\alpha^{3.7}$

--MEDI

$-\alpha^{20.5}$

--MEDII

α^{5nt}

α^{PolyA2}

δ -thal 2%

(Thr \rightarrow Ile) C4

(Ala \rightarrow Ser) C27

(Arg \rightarrow Cys) C116

(AG \rightarrow GG) IVS II

(Leu \rightarrow Pro) C141

Abnormal Haemoglobins

Hb S

Lepore

Setif

Knossos



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Blood transfusion Services

- Appointment is given for cross matching
- After the consultation with the doctor and according to the follow up protocol the needed tests are decided
- After blood donation and Hb results and according to the patient's availability, preference and health situation the date of blood transfusion and the amount of blood, that is planed to transfuse, is decided by the doctor



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Blood transfusion Services (continue)

- The patient is informed by the clinics' nurses, through SMS, about his Hb results and the date of planned blood transfusion
- The blood for transfusion is prepared in the blood bank in N.G.H. and is sent to our clinic



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Blood transfusion Services (continue)

- On the day of blood transfusion and when the blood is ready the patient is informed through SMS by nurses, that the blood is ready
- Before transfuse the blood, all the necessary information is transmitted to the patient's records, by the clinic's nurses



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Chelation Treatment Services

- All the three approved drugs are used for chelation treatment , as monotherapy or combination
- According to the patient's situation, haemosiderosis' data, together with the patient , the chelation treatment is decided



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Chelation Treatment Services

(continue)

- Education of patients and the parents (for the children), by the staff about the chelation treatment, as well on practical issues
- Written information and instructions are given
- Desferal is given i.v.
- Use of port-a-cath (not now)
- Check compliance and interfere when needed
- Follow safety and efficacy of the treatment

Management of Splenectomy

- Decision about splenectomy according to our protocol (only when persistent hypersplenism and symptomatic splenomegaly)
- Vaccination before splenectomy
- Education of patients about possible complications and their prevention
- Follow up after splenectomy



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Follow up protocol

- The protocol has been decided with all staff of the clinic, according to International and TIF Guidelines
- The protocol's realization is responsibility of doctor in charge
- Set the appointment
- Plan and set test
- Tests provided in the clinic
 - All blood tests
 - OGTT and other specific tests GH test,



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Management of complications

- Investigation and diagnosis of complications, with close collaboration with the specialists,
- Treatment realization and diagnosis of it's side effects
- Set follow up appointments
- Compliance with the treatment



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Bone Marrow Transplantation

- Not in Cyprus, patients are refereed abroad and the cost is covered by the government
- Clinic role consists of giving information and helping patients/parents to decide about BMT
- Organize the appointment and referral abroad
- Inform patients and his family about procedures of B.M.T. and the risks
- Follow patients after BMT



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Psychological support

- Twice a week by a psychologist
- Medical and nurse staff



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Special Services

- Short hospitalization
- Investigation and Treatment of all health care problems



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Special conditions in Thalassaemia

- Patients are required to visit Thalassaemia Unit and receive medical treatment and counsel with their physicians on a frequent basis, so that specific relationships are developed



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Special conditions in Thalassaemia

- Patients consider clinic as a second house
- Special conditions must be provided in order they feel comfortable to express their feelings, thoughts, worries, treatment problems and non-compliant issues
- However, limits should not be crossed concerning doctor-patient relationship



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Projects

Thalassaemia clinics participate in different multicenter, local or international projects such as :

-ITHANET

-ENERCA

-DEEP

-THALAMOSS



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Projects (continue)

- Gene Therapy
- Chemoinformatic solutions for the identification and optimization of agents for the treatment of thalassaemia
- Genotype/phenotype correlation studies for HbH-disease patients and all the β - thalassaemia patients in Cyprus
- Cordelia



Aims

- Quality of care
- Patient center care
- Continuity of care
- Satisfy patients' perspective
- Continuous education of staff
- Provide care according to the latest data
- Equality in access of the clinic services



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Mission of the clinic

- Improve the health of patients
- Decrease morbidity and mortality
- Improve patients' quality of live



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Marital Status

Nicosia Thalassaemia Clinic

Nicosia Thalassaemia Clinic												
Male					Female				Total			
	Married	Divorced	Parents	Not Fertile	Married	Divorced	Parents	Not Fertile	Married	Divorced	Parents	Not Fertile
Number	73	16	80	9	99	15	98	15	172	31	178	24
%	82	18	90	10	87	13	86	14	85	15	88	12
Total	89				114				203			



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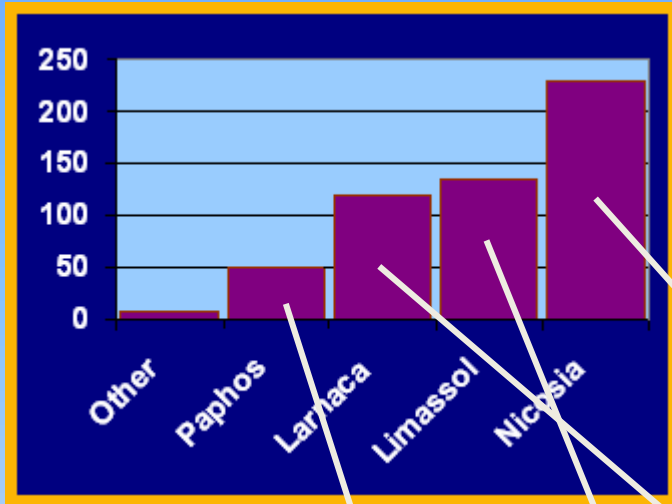


Pregnancies of women with thalassaemia in Cyprus

Clinic	Number of Women	Number of Pregnancies	Number of born Children	Twins	Triplets
Nicosia	96	151	167	14	0
Limassol	31	48	53	3	1
Larnaca	38	55	68	5	1
Pafos	12	20	21	1	0
Total	175	272	307	23	2

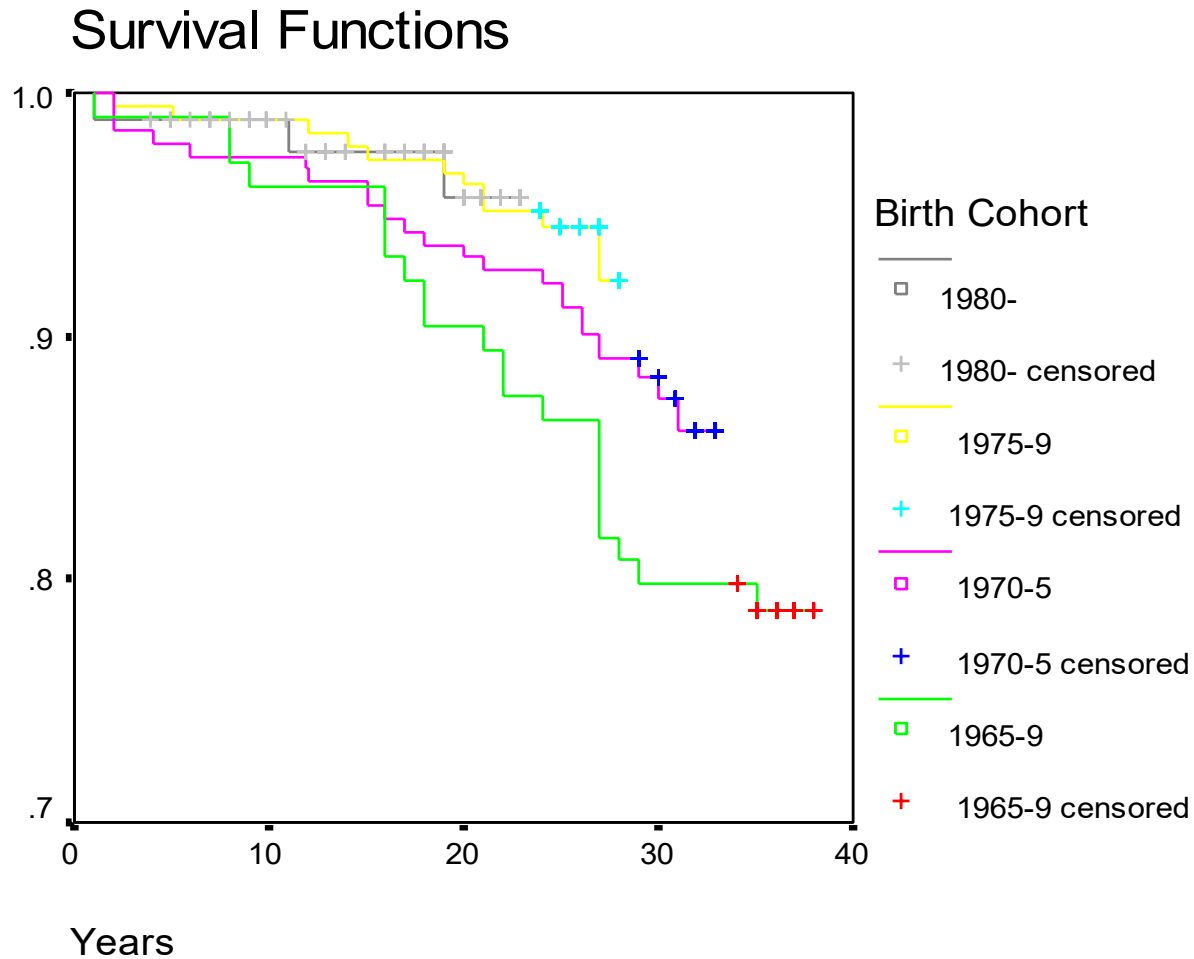
Cyprus Study

M.Angastiniotis
S. Christou,
E. Pangalou,G.Skordos,
N. Pavlides, K. Simamonian.
M. Psiloines, M. Hadjigavriel
M. Sitarou
A.Kolnagou



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Cyprus thalassaemics: overall survival

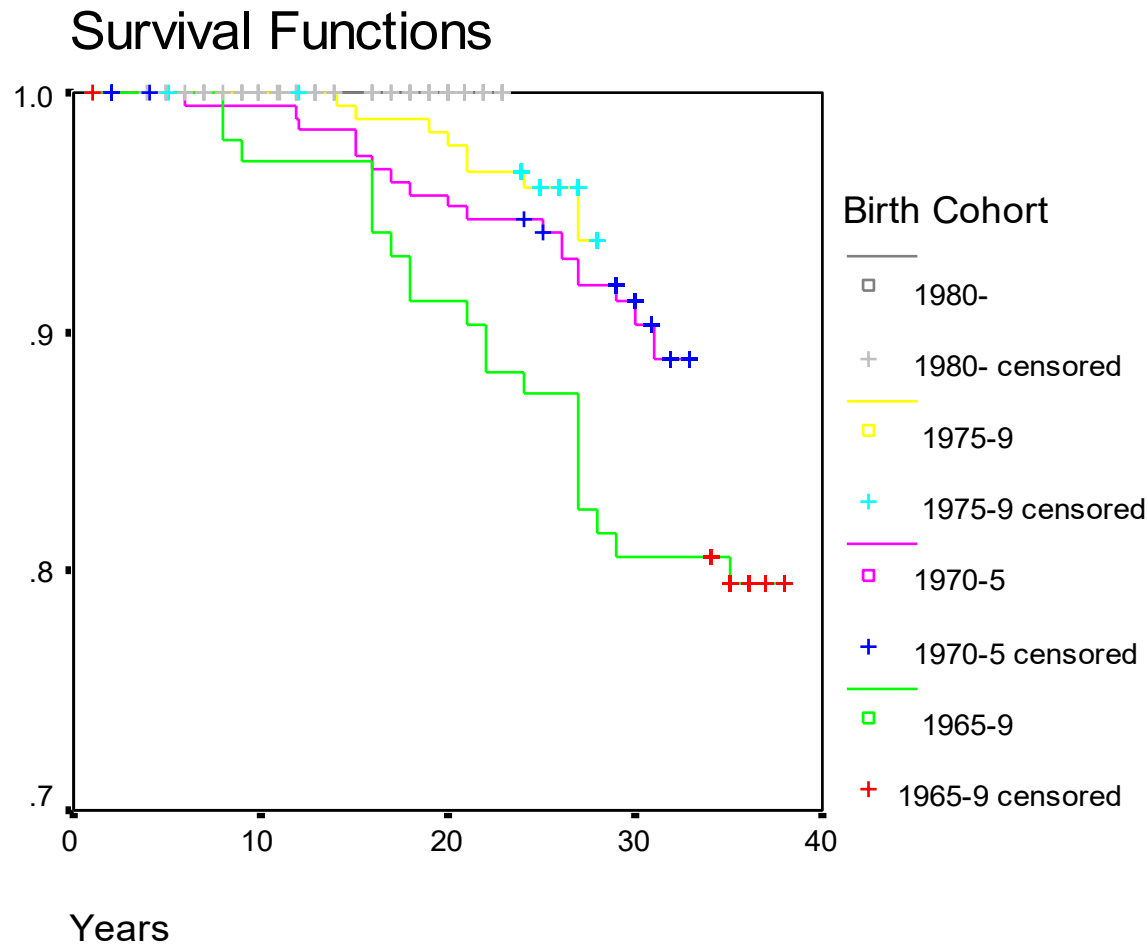


1965-9 n=104
1970-4 n=192
1975-9 n=184
1980- n=92

Logrank 7.4
p=0.06



Cyprus thalassaemics: Thalassaemia-related mortality

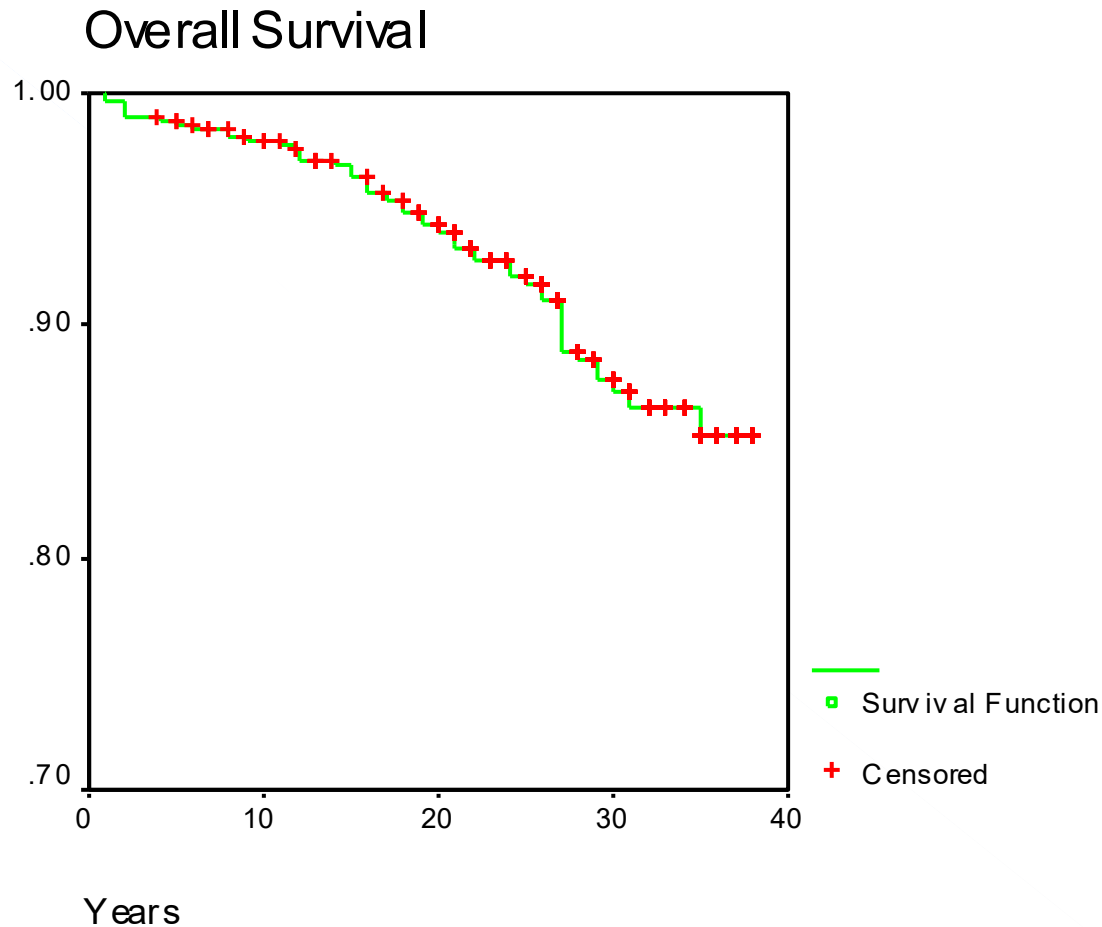


1965-9 n=104
1970-4 n=192
1975-9 n=184
1980- n=92

Logrank 13.3
P=0.004

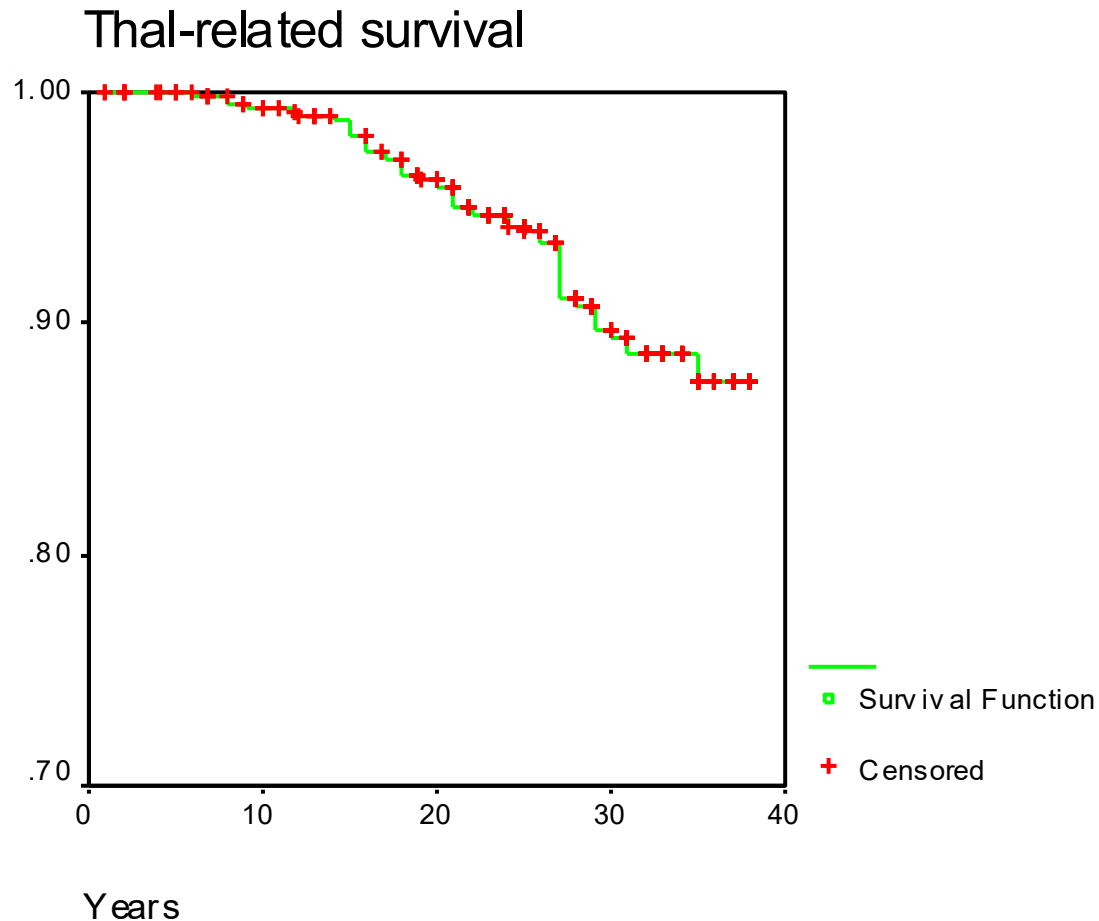


Cyprus thalassaemics 1965-cohort: Overall survival



N=572
Events 60

Cyprus thalassaemics 1965- cohort: Thalassaemia related survival



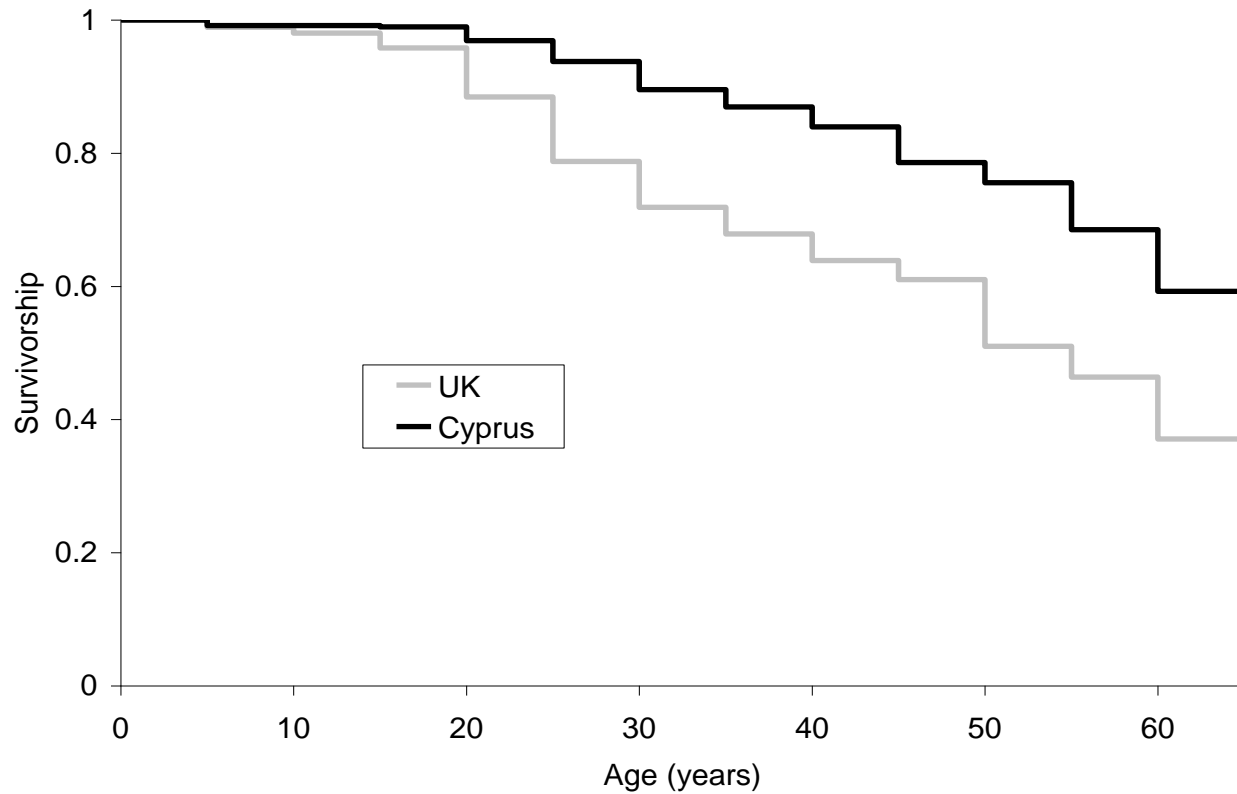
N=572
Events:47



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Survival in UK and Cyprus



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Acknowledgment

First, a big thanks to all our patients!

Ministry of Health

Director of the Hospital

The medical staff at the clinic

Dr. Evdokia Pangalou

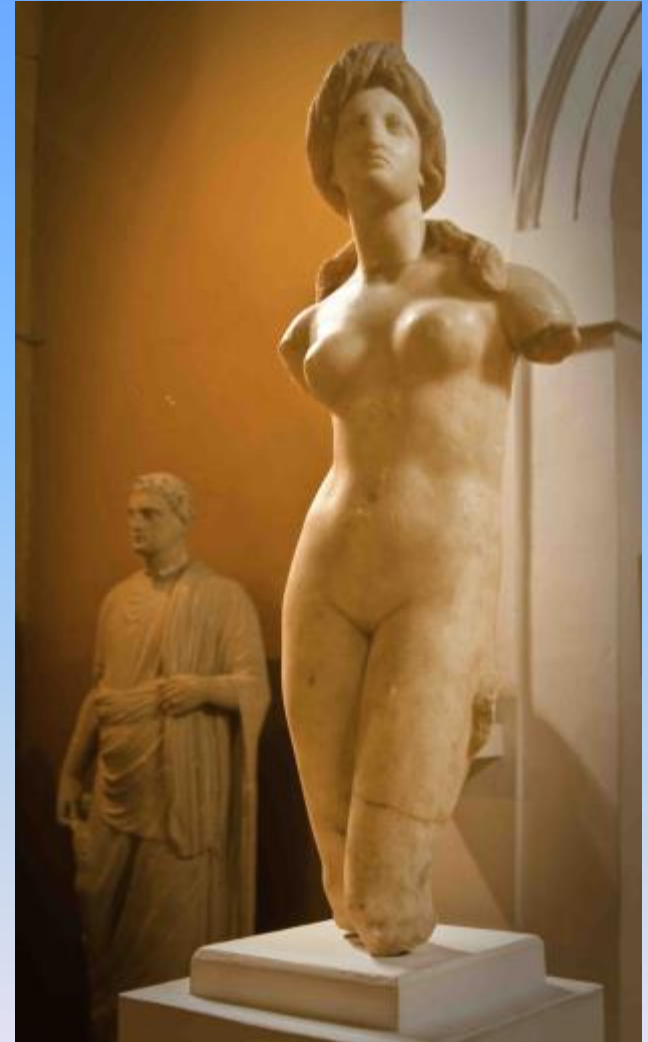
Dr. Irene Savvidou

Sister Theopisti Loizou

Staff nurses Christina Papadopoulou, Christina Ioannou, Georgia Charalambous, Andri Charalambous, Christina Petrou, Chrystalla Chrysanthou, Stella Andreou, Irene Saxiate

All the doctors collaborate with us

Thank you for your Kind attention



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