PROGRAMUL DE COOPERARE ELVEȚIANO-ROMÂN
SWISS-ROMANIAN COOPERATION PROGRAMME

Addressing the barriers to pediatric cancer management

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Outlines

I. Pediatric cancer –one of thousands of rare disorders

II. Pediatric cancer in the world

III. Pediatric cancer in Romania

IV. Challenges ….. Barriers

V. Solution

VI. Future

I.Pediatric cancer –one of thousands of rare disorders

1. Epidemiology
2. Outcomes of therapy
3. HTA in pediatric oncology

Rare diseases – orphan diseases

- **6 - 8% of population (EU) =30mil. in EU; <245.000**
- **5000 – 8000 rare diseases**
- **30% - die before the age of 5**
- **75% - affect children**
- **80% - genetic diseases**
-

Rare	Ultra rare
USA - < 1/1.500~6,6/10.000 EU - < 5/ 10.000 Japan - < 4/ 10.000	< 2.000-5/10.000 <0,2/ 10.000

(ORPHANET -2014)

Incidence of PC (/ 100.000/ yr)

0-14 yrs -13-15

0-19 yrs -18-20

15-39 yrs -138,6

>39 yrs -2.053,8

Annual rate of PC/ 100.000/ yr

0-4 yrs -16,6

5-9 yrs -9,3

10-14 yrs -9,5

0-14 yrs -13-15

(SEER -2014)

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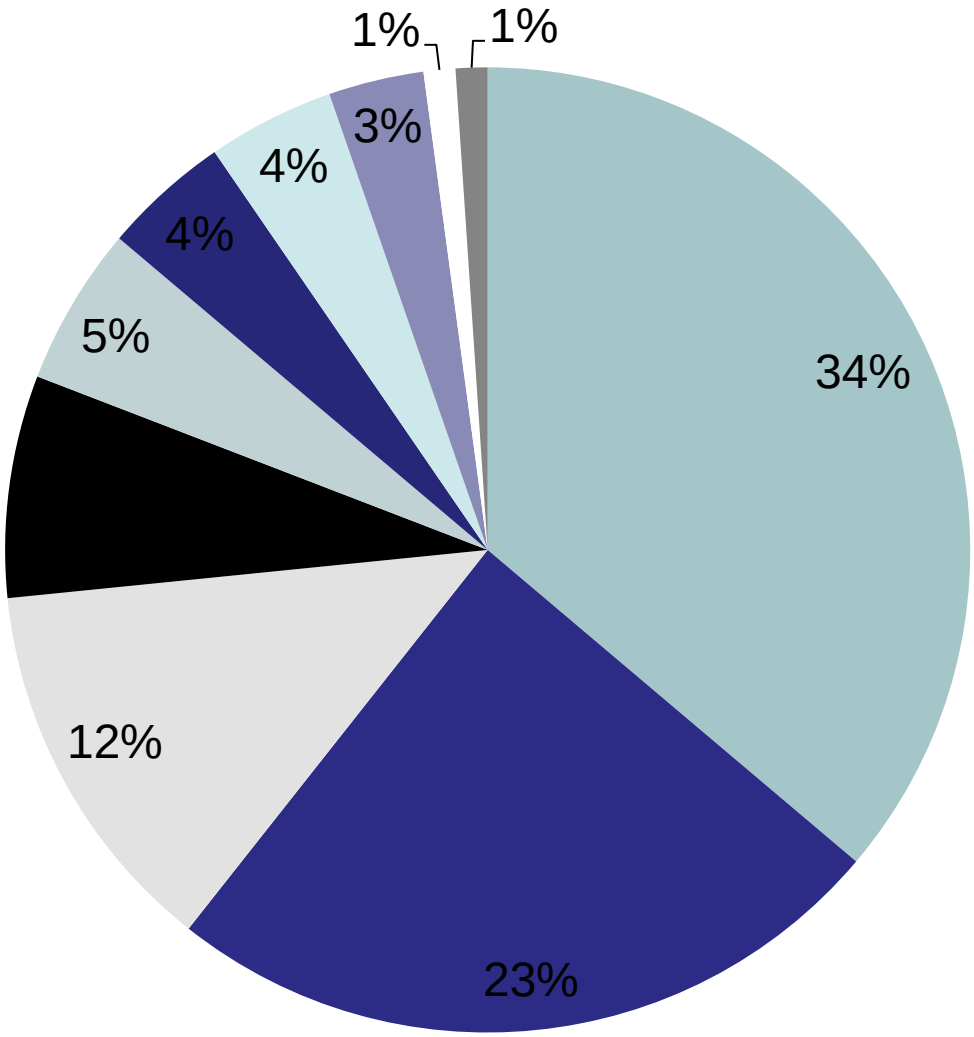
Types of cancer



- Leukemia 34%
- Brain t. 23%
- Lymphomas 12%
- Neuroblastoma 7%
- Wilms t. 5%
- NHL 4%
- Rhabdomiosarcoma 4%
- Retinoblastoma 3%
- Ewing s. 1%
- Germ cell t. 1%

Rare cancers (<3%)

- Pancreatobl
- Meningioma
- astomaMelanoma
- Pleuro-pulmonary t.
- Hepatic t.
- Nasopharyngeal t.
- Oropharyngeal t.
- Breast t.
- GI tract t.

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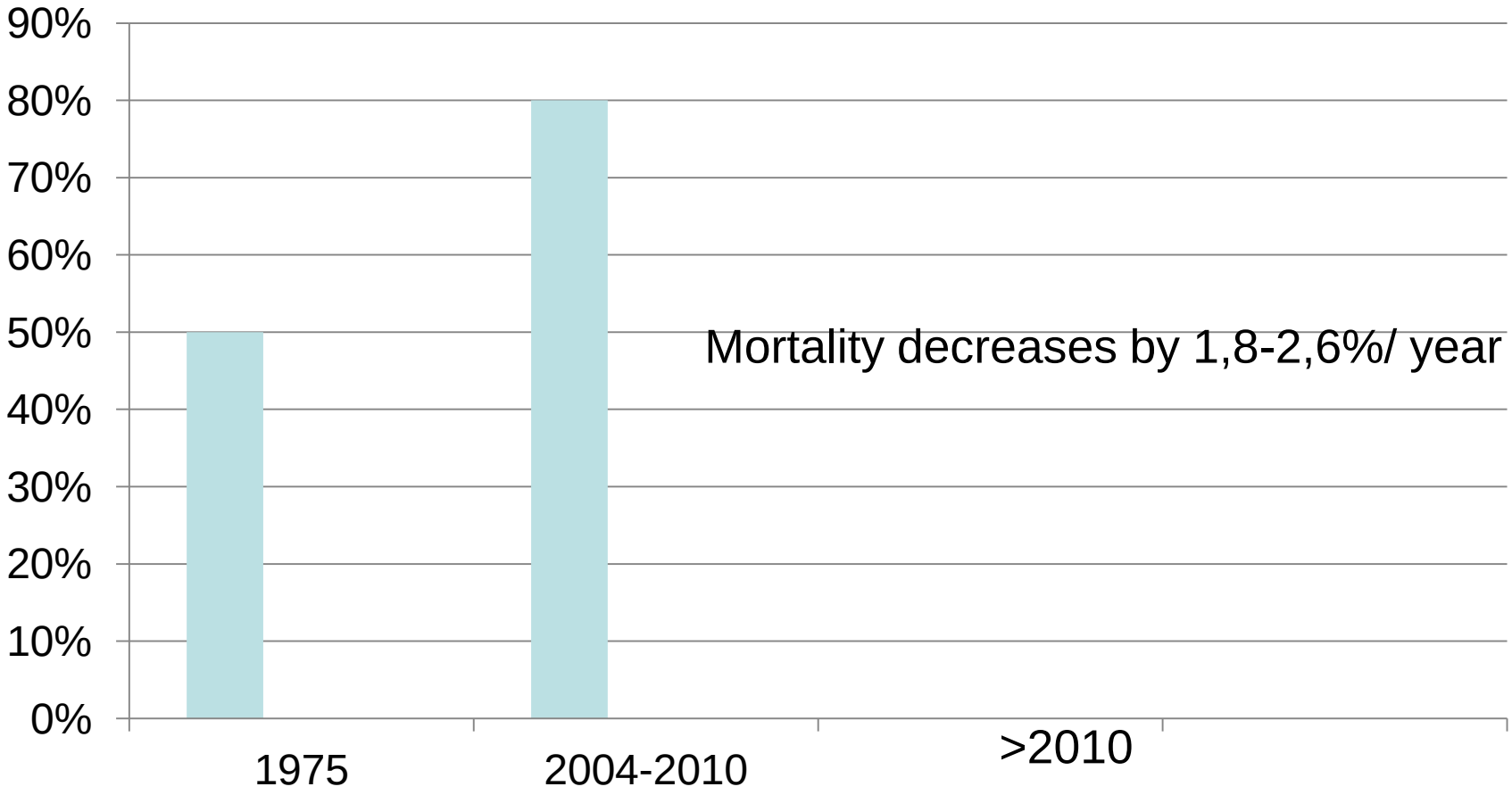
Outcomes



5 yrs OS in pediatric cancer (Howlader N -2014)
Long term survivors – 380.000 in USA (2010) – (Ward E -2014)

- **“Resources are scarce**
- **Wants/ needs are infinite**
- **Choice is inevitable**
- **No direct market for health**

“ The benefit evaluation obtained from employing resources in their best alternative use is mandatory”

(A.Briggs -2012)

Escalating budget pressures

-payers (health insurance)	-physicians (care givers)
-budget holders (health companies)	-patients (care demanders)

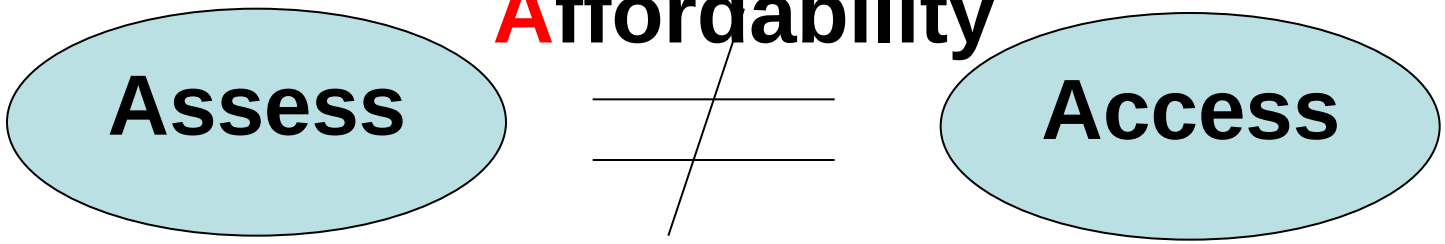
Availability

↓

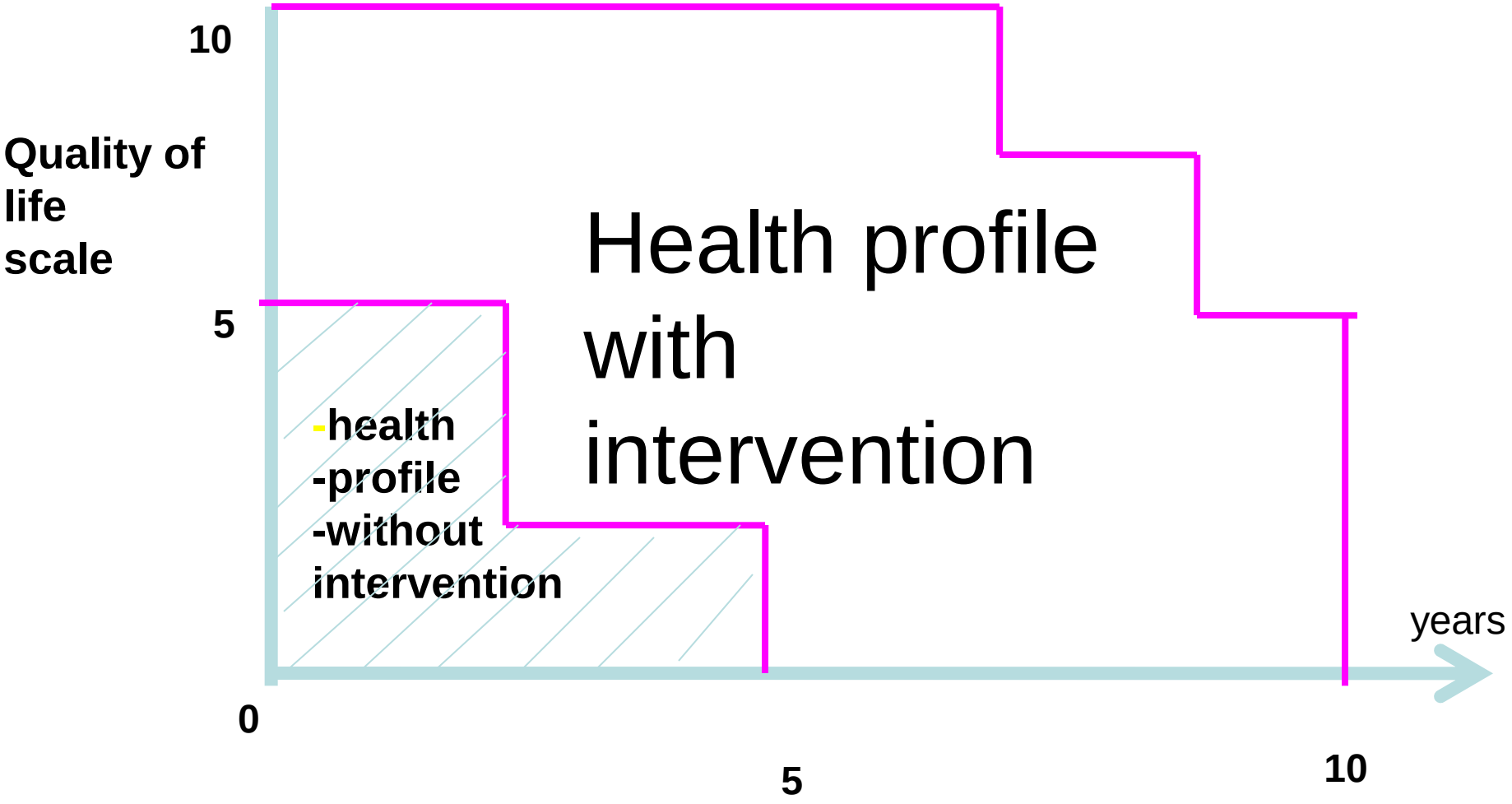
Accessibility

↓

Affordability



QALY gains


10
Quality of life scale
5
0
Health profile with intervention
-health
-profile
-without
intervention
years
5
10

Incremental Cost-Effectiveness Ratio = ICER

$$ICER = \frac{C1 - C0}{E1 - E0} = \frac{cost}{QALY}$$

C1 =costul noii tehnologii
C0 =cost fără
E1 =rezultatul tratamentului
E0 =rezultat fără tratament

QALY (quality adjusted life-years)
(evaluare: VAS –visual analogue scale
TTO –time trade off
SG –standard bet Gamble)

QALY

QALY = Utility scale x years of live saved (life score)

T-I	**0,9**	**x**	**10**	**=**	**9**
T-II	**0,5**	**x**	**4**	**=**	**2**

7 years gained

Cost-effectiveness

T-I –costs = 90.000 €

T-II -costs = 20.000 €

70.000 €/ 7 years

Cost/ QALY gained = 10.000 €

Considered acceptable

25.000 – 34.000 €/ QALY → 52.000 €/ QALY

(D.NOON E. -2010)

Threshold of ICER

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Country	Accepted value (E)
UK	29.500 – 44.250
Netherlands	20.000 – 80.000
Sweden	35.000 – 55.000
Germany	20.000 – 40.000
USA	50.000 $
Canada	20.000 – 100.000
Australia	23.000 – 43.000

- **“No child should die of cancer**
- **Children with cancer should be treated”**

(SIOP, Pan Care -2014)

II.Pediatric cancer in the world

1.General data

2.Challenges

3.Successes

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- **Adult cancer diagnosed/ 2014 -1.368,030**
- **Pediatric cancer diagnosed/ 2014 -15.780 (0,88%)**
- **Pediatric cancer death/ 2014 -1.960**
- **COG sponsored clinical trial -4.000 (29-50%)**

(SEER -2014)

Budget for cancer

- **Overall -4800 billions $**
- **Pediatric -173 millions $ =(3%)**

(0-20 yrs)

(SEER -2014)

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Challenges

-Cancer in Kids is Not Profitable

-Kids Do Not Vote

-Kids'Cancers a Are different

-Kids'Cancers Behave Differently

-Too Few Kids

-Kids Get the Hand-Me-Downs

-Kids Are Not Little Adults

-Limited Preclinical Models for Kids'Cancers

-Too few Formulations for Kids

-Ethical Considerations with Kids

(J.Boklan -2006)

Successes

-Kids' Well-Oiled Clinical Trial Machines

-Kids Have Parents

-Response Assessment Easy

-Kids Are (Otherwise) Healthy

-Kids Make Hand-Me-Down Fit

(J.Booklan -2006)

5 yrs OS survival

	0-14 years	0-19 years
1975	58%	61,5%
1985	68,1%	70,5%
1995	77,4%	77,7%
2010	83,1%	83,5%

(SEER -2014)

III.Pediatric cancer in Romania

1.Economical background

2.Results

3.Difficulties …..barriers …….

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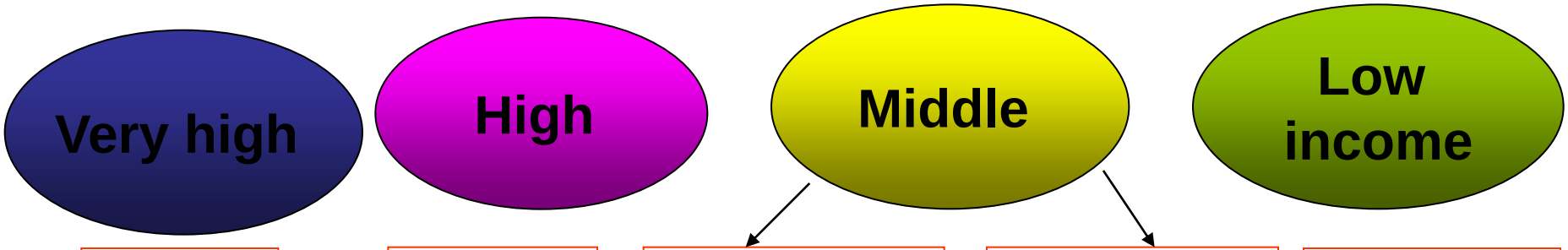
Economic classification (income groups GNI/cap/y/$) (W.B. – 2012)



France
Germany
Great Britain
Sweden
USA
Japonia

Czech
Slovak
Slovenia
Croatia

Bulgaria
Macedonia
Montenegro
Serbia
Albania
BH
Hungary
Romania

developing economics

GNI/cap /y(formerly GNP) converted in US $ (2012)

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	GNI/cap/y	HE/cap/y
Albania	4090	255
Bosnia Hertegovina	4650	493
Bulgaria	6870	522
Croatia	13290	1138
Czech R	18130	1500
Greece	23260	2864
Hungary	12390	1085
Moldavia	2670	224
Polonia	12670	899
Romania	8420	500
Serbia	-	439
Slovakia	17170	1534
Slovenia	22270	2218
X	11,092	901,3
X (WE)	52445	5556,4

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Health expenditure (%)

Albania	6
Bulgaria	7,3
Bosnia Hertegovina	10,2
Czech R.	7,4
Hungary	7,7
Macedonia	6,6
Moldavia	11,4
Greece	10,8
Croatia	7,8
Montenegru	3,3
Polonia	6,7
Romania	5,8
Slovenia	3,1
Slovakia	8,7
X	8,23
X (WE)	10,15

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Infant mortality/ 1000/y

Albania	13
Bosnia Hertegovina	7
Bulgaria	11
Croatia	6,16
Czechia	3
Greece	4
Hungary	5
Moldavia	14
Polonia	5
Romania	11
Slovacia	7
Slovenia	4,17
X	10,23
WE	3,71

(WB -2012)

Incidence of tuberculosis/ 100.000/ year

Albania	13
Bosnia Hertegovina	49
Bulgaria	35
Czech R.	7
Hungary	18
Romania	101
Greece	4
Moldavia	161
Serbia	16
X	46,6
WE	8,14

Introducere

- **90% din copiii cu LAL sunt supravietuitori de lunga durata**

- **1996 – imunofenotipare**
- **1998 – citogenetica conventionala +FISH**
- **2001 – biologie moleculara**

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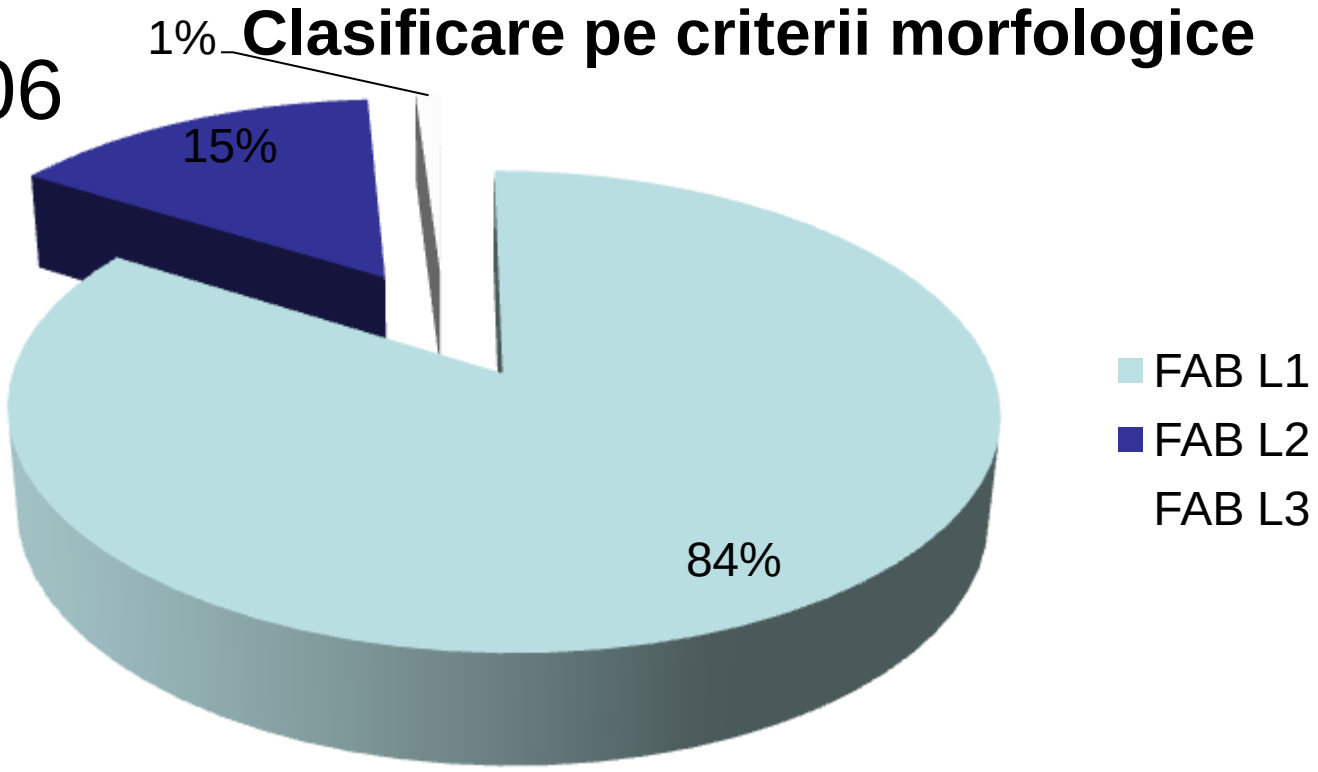
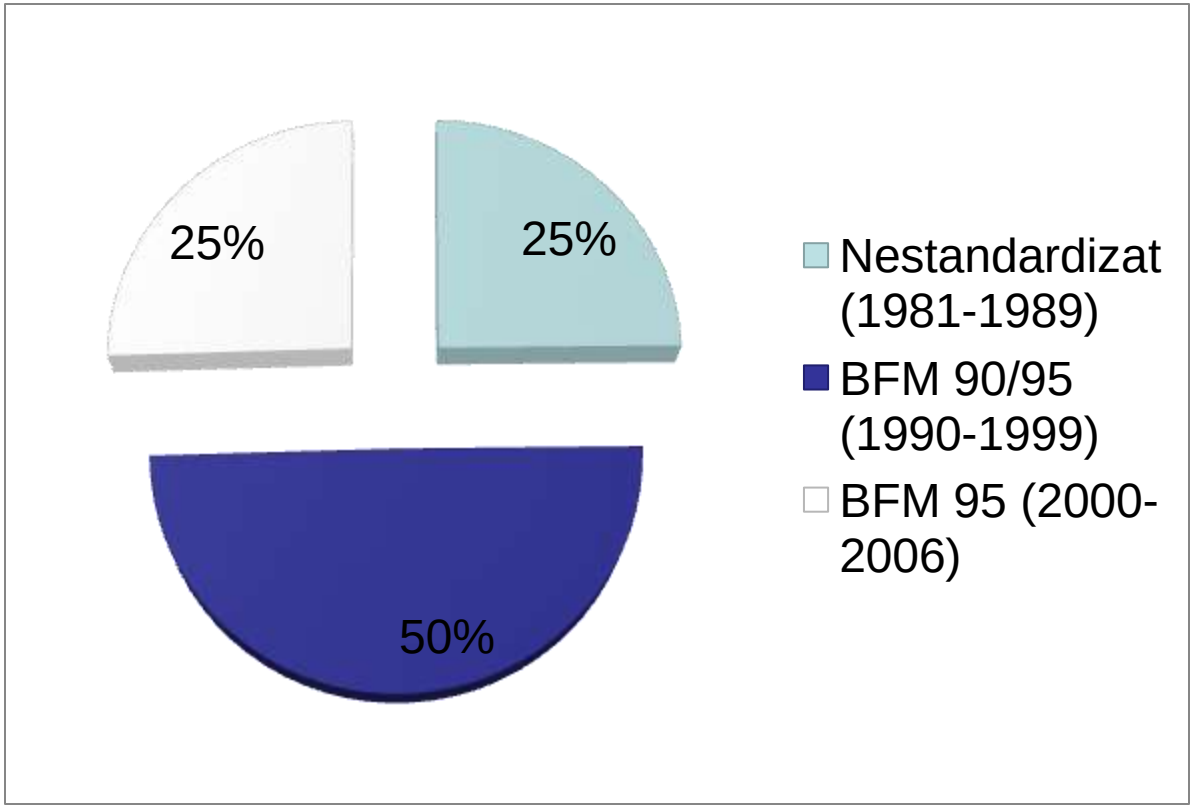
Material si metoda

- Studiu restrospectiv – 314 pacienti (0-18 ani)
- 1981-2006



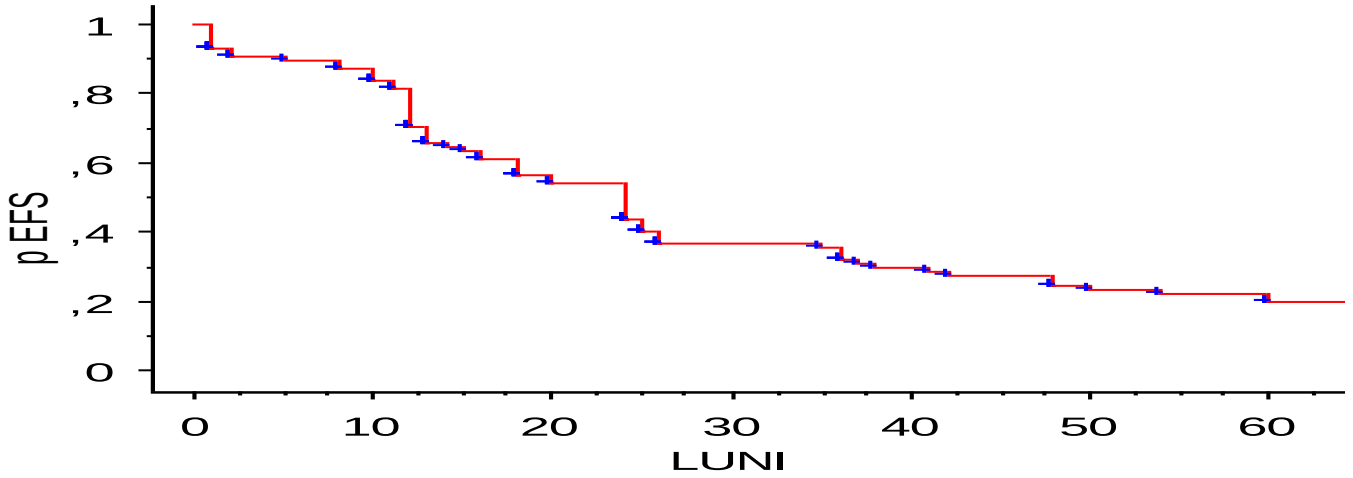
Material si metoda

- **Protocoale de tratament utilizate**



Rezultate

- pEFS la 3 si 5 ani la pacientii tratati nestandardizat in perioada 1981-1989

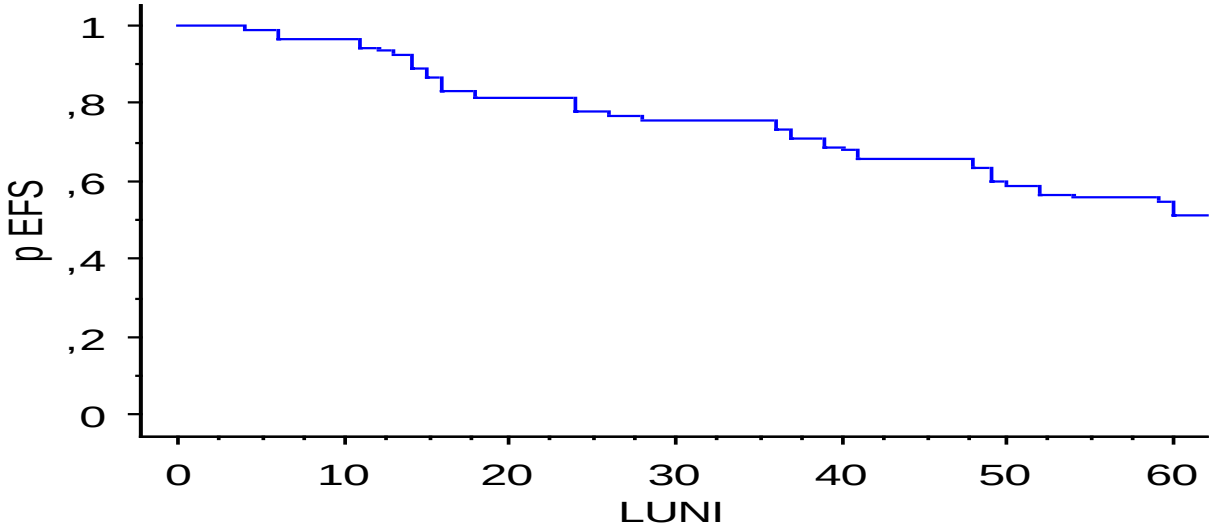


EFS LA 3 ANI ~ 40%

EFS LA 5 ANI – 20%

Rezultate

- pEFS la 3 si 5 ani la pacientii tratati conform protocoalelor BFM 90/95 in perioada 1990-1999

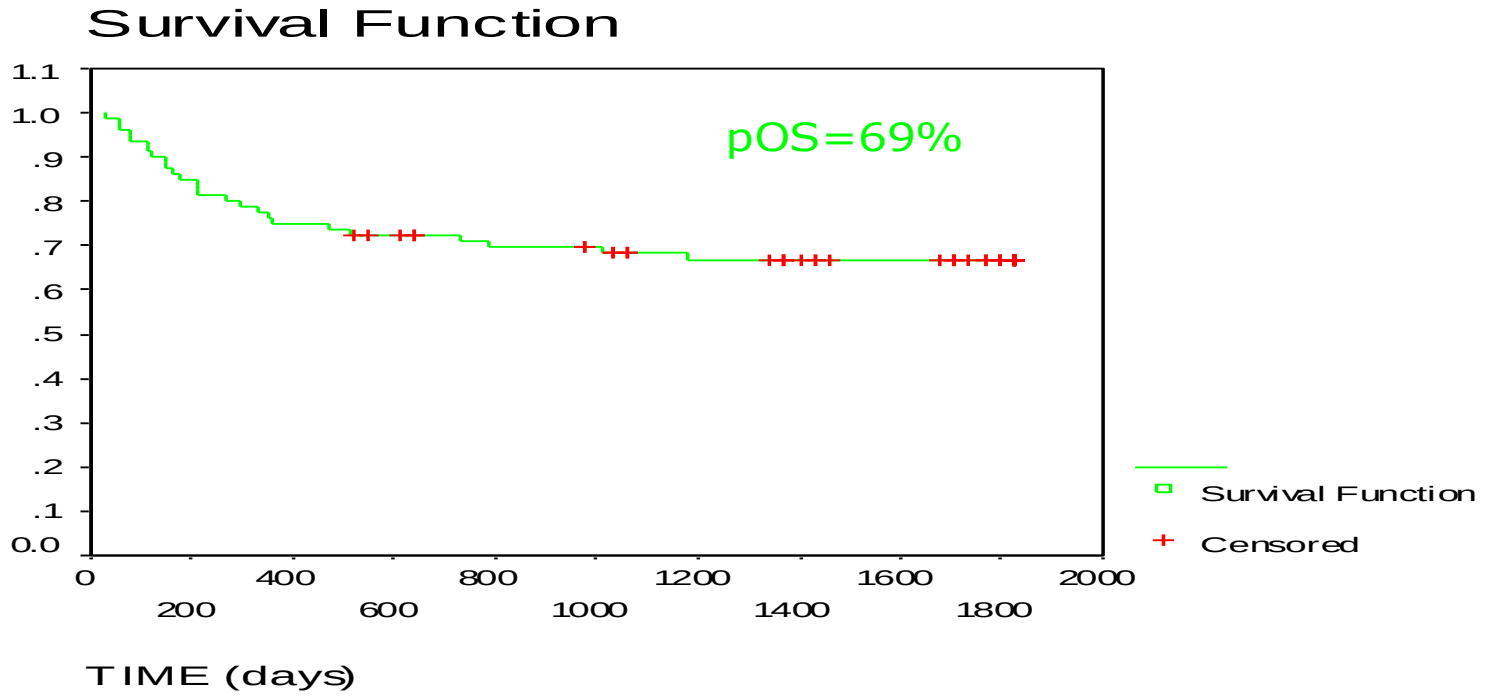


EFS LA 3 ANI ~72%

EFS LA 5 ANI ~ 52%

Rezultate

- pOS la 5 ani la pacientii tratati conform protocolului BFM 95 in perioada 2000-2006



IV.Challenges ……
Barriers

1.Individual level

2.Local level

3.National level

4.International level

- **Individual level**

-lack of postgraduate training in pediatric onco-hematology

-the existent specialists (pediatricians, oncologists, hematologists, being granted arbitrary on some criteria: experience, working place)

-unfavorable impact on the professional skills/ knowledge of the small number of specialists

-demotivation (lack of correlation between quantity/ quality of work and the salary in comparison with other fields)

- **Local level**

-lack of a team for comprehensive approach of pediatric cancer(diagnosis, surgery, chemotherapy, radiotherapy, monitoring, psychosocial-support)

-restricted number of care givers (negative impact on inter-centers cooperation, research, statistics)

- **National level**

-lack of functional society with a loud voice speaking into the interest of patients

-lack of national registry

-lack of working groups

-lack of national protocols

-lack of a functional pediatric Onco-Hematology journal

-lack of a formally designated network of pediatric oncology centers (objective criteria !!!) (not wish, not will, but doing things)

-lack of a real cooperation (evaluation, statistics, research)

-limited/ discontinuu access to some diagnostic, therapeutical measures procedures

Difficult or lack of access

Cause	Medication
Not on market	Thiothepa –Amp 15mg Eldesine BCNU Melphalan Amsacrin –Amp 50mg Treosulfan Daunoblastin –Amp 20mg Timoglobulina (horse) Trimetoprin (IV) Tavegyl (IV) Tranexamic Ac. Defibrotide Thalidomid Micofenolat (IV) Tacrolimus (IV) Cyclosporin (IV) Pentamidin (IV) Foscarnet Cidofovir

Difficult or lack of access

Cause	Medication
Lack of imbursement by PN	Erwinase Oncaspar Procarbazine Lomustin Busilvex –A
-Lack of pediatric formulations	Cyclosporine –Amp; -Sirop Dacarbazine
Off label usage	Rituximab Eltrombopag

- **International level**

-lack of participation in international study groups

-lack of clinical trials in pediatric oncology

-spread-out of the opinion disqualifying our activity with dissatisfaction and loss of confidence

-promotion of actions favoring transborders medical assistance (non-equity of access, very high costs)

V. ……Solutions

- **Start of postgraduate training in pediatric onco-hematology**
- **Create of a network of regional centers with standards of expertise for modern diagnosis, therapy and monitoring of cancer (using objective criteria not based on wish, will –but on capability of doing this comprehensive work, not forgetting the physical barriers to care)**

- **Establishement of a motivating structure and salaries ,which should make possible**

–national registry

-national working groups

-national protocols

-national evaluation …. and

-prevent abandon of the field/ country

- **Proper solutions for access to “orphan drugs”**

-to right medication

-in right quantity

-in right dosage

-in right moment

With creation of in-time-accessible “national emergence deposit”

***registration**

***market – authorization**

***imbursement –of orphan drugs or formulations**

- **Incentives for participation in international study groups /conferences/ clinical trials**
- **Fostering research (EU fonds)**
- **Inacting several European regulations, not overtaking from economically powerful EU countries, but applying them to our possibilities**
- **Increase of HTA responsabilyties in the field**

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VI.....Future

.....

- **Remove barriers to diagnosis, care and monitoring of our patients, obstacles to the real chance of surviving, by supporting our needs into the favor of our small, silent, patient, patients group**
- **They deserve a better future ……. the cure of their cancer**

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