Haemophilia in Europe with respect to clinical outcome, quality of life and care resources (socio-economic studies)

Regional Haemophilia Meeting
Esfahan Iran
April 19th-20th, 2009

Wolfgang Schramm
Ludwigs Maximilians Universität München
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Klinikum der LMU

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IHTC CCC

HÆMORRHAGIC DIATHESIS.

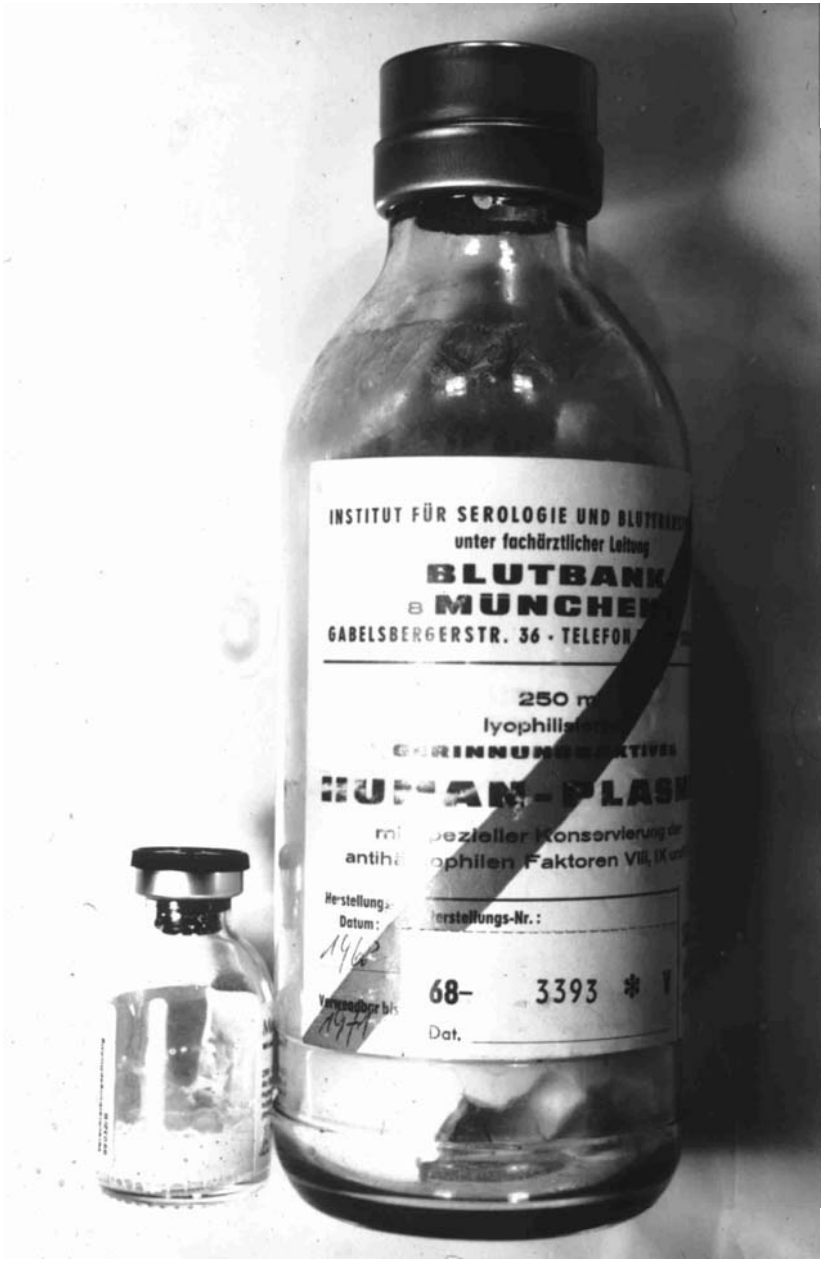
SUCCESSFUL TRANSFUSION OF BLOOD.

By SAMUEL LANE, *Esq., Lecturer on Anatomy and Surgery in the St. George's School, Grosvenor-place, Hyde-Park Corner.*

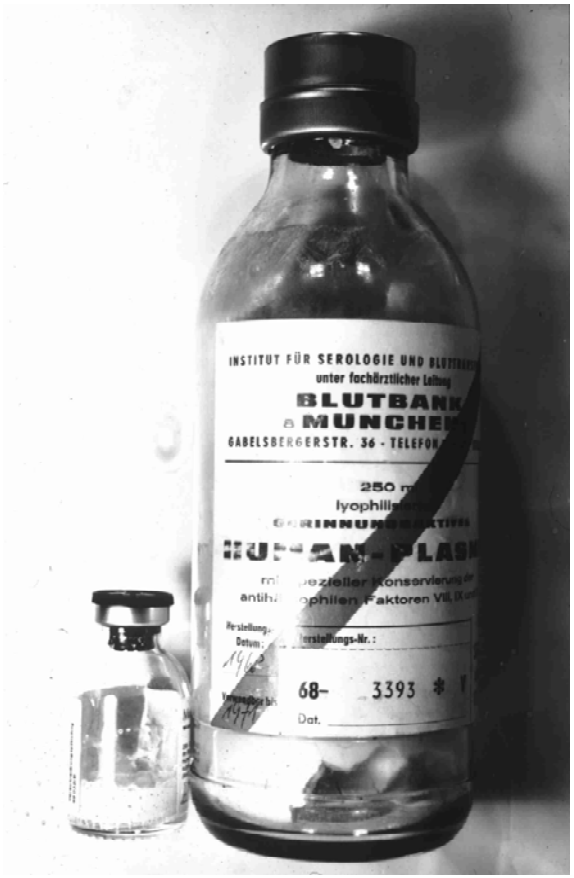
To the Editor of THE LANCET.

SIR:—Allow me, through the medium of your Journal, to place on record a success-

From transfusion of blood to infusion of factor concentrates.



Haemophilia treatment: factor VIII substitution
Progresses in Haemophilia treatment 1953 - 2005:

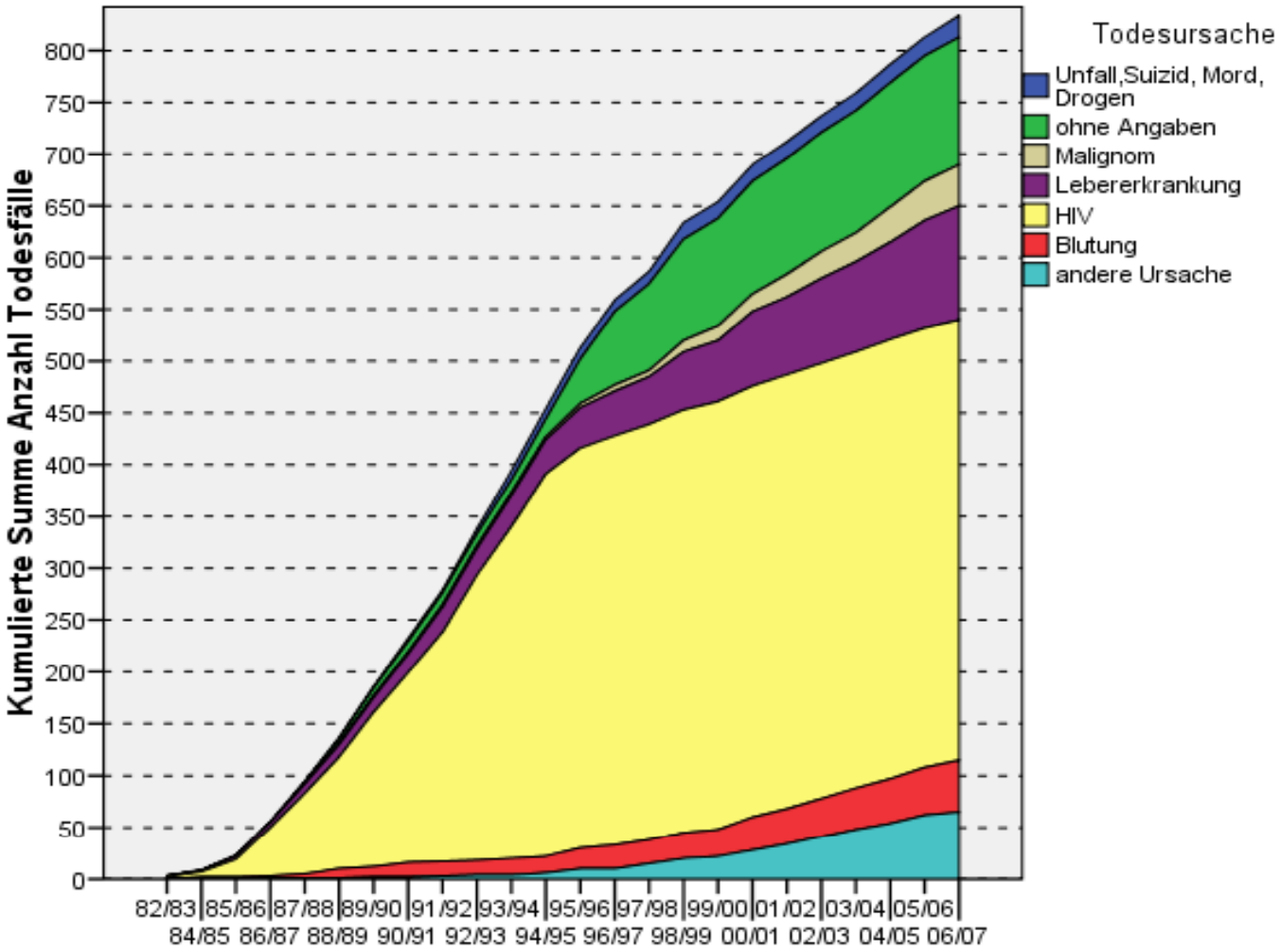


- **Industrial production of factor concentrates**
- **Prophylactic therapy with factor concentrates in children and adolescents**
- **Production of recombinant factor concentrates**

Benefits

- **Treatment and avoidance of bleedings**
- **Avoidance of infections (HBV, HCV, HIV)**
- **Less disablilities, chronic complications**
- **Better Quality of Life**
- **Social integration**

Haemophilia: Cause of Death > 1982



Causes of Death
1978 – 1983 and 2002 – 2007

	1978 – 1983 (n = 60)	2002 – 2007 (n = 104)
Bleeding	51 %	17 %
Liver disease	15 %	28 %
Malignant tumor	10 %	13 %
Other internal diseases	12 %	25%
Accident, Suicide, murderd, Drogen	12 %	11 %
HIV	0 %	6 %

Haemophilia Care - European perspective

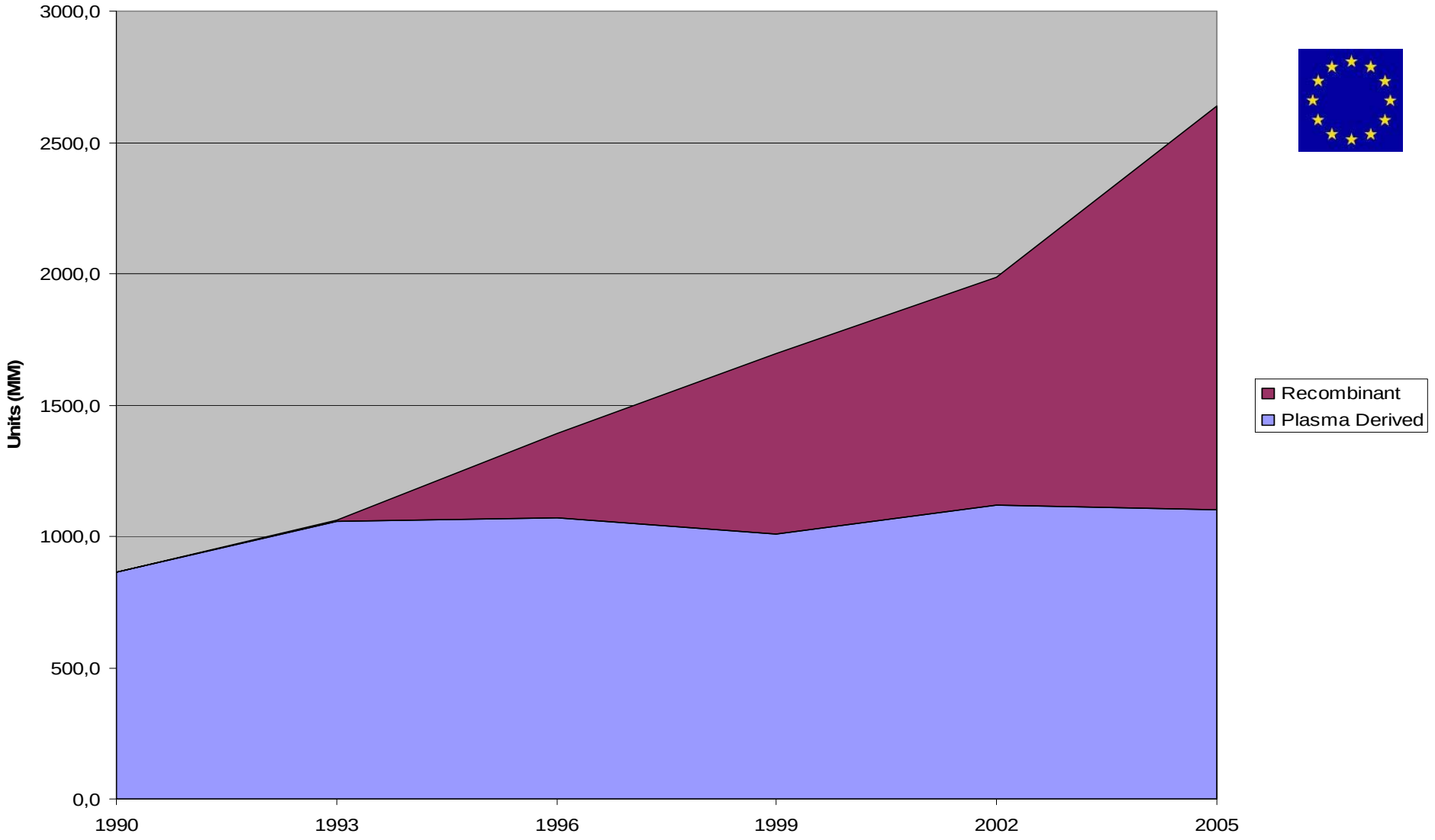
Wildbad Kreuth Initiative 1999

Recommendation 128

"Adequate amounts of coagulation factor concentrates for the treatment of patients with haemophilia and related disorders should be available in each Member State. Quantities of both plasma-derived and recombinant products should be maintained, although it is recognised that recombinant products could gradually supplant plasma-derived ones. Individual patient preferences should be taken into consideration when choosing products."

Schramm W.: Conference Proceedings ISBN 3-00-005705-6

F VIII+IX: Units (MM) 1990-2005 Plasmaderived + Recombinant



Europ social econ. Study ESCHQoL pers. com. P.L.Robert MRB

Clinical Outcome: Prophylaxis in Haemophilia Treatment

- Twenty-five years‘ experience of prophylactic treatment in severe haemophilia A and B

  (Nilsson et al., J Intern Med 1992; 232: 25-32)

  - 60 severe haemophiliacs A (n=52) and B (n=8)
  - age: 3-32
  - treatment start at age of 1-2 years
  - 25-40 IU/kg body weigth three times a week for haemophilia A, 25-40 IU/kg body weigth twice a week for haemophilia B
  - 5-year period
  - orthopaedic and radiological joint scores were evaluated according to recommendations by the WFH

=> 3-17 years: 29 out of 35 showed patients joint scores of zero

The oldest group had only minor joint defects.

All 60 are able to lead normal lives

Clinical Outcome: Prophylaxis in Haemophilia Treatment

A longitudinal study of orthopaedic outcomes for severe factor-VIII-deficient haemophiliacs. The Orthopaedic Outcome Study Group

(Aledort LM et al., J Intern Med 1994 Oct; 236 (4); 291-299)

- **multicenter (21), uncontrolled, prospective, 6 years**
- **477 patients under 25 years (mean 13.5 ± 6.6), severe Haemophilia A, no inhibitor**

→ **Bleeding episodes**
→ **Joint bleeds and sites**
→ **Use of prophylaxis**
→ **Factor consumption**
→ **Evaluation of elbows, knees, ankles**
→ **Days missed from work and / or school**
→ **Days hospitalized**

Clinical Outcome
Prophylaxis in Haemophilia Treatment

A longitudinal study of orthopaedic outcomes for severe factor-VIII-deficient haemophiliacs. The Orthopaedic Outcome Study Group

(Aledort LM et al., J Intern Med 1994 Oct; 236 (4); 291-299)

Variable	> 45 Weeks	No specific prophylaxis	p (U-test)
Number of patients	66	411	
Average (year 6 – year 1) score	1.00	3.05	0.002
Average start score	2.69	6.59	0.00001
Average final score	3.70	9.64	0.00000
Average joint bleeds	5.65	16.5	0.00000
Average age	12.5	13.7	0.134
Average dose	2772	1038	0.0000

Over 45 weeks / year prophylaxis physical examination data

Clinical Outcome
Prophylaxis in Haemophilia Treatment

Schramm, W. Experience with prophylactic treatment in Germany. Royal Society of Medicine Round table series 1991, 25, 12-17.

Table 1. Description of the Hemophilia Cohort

	Treatment			
		On-Demand		
	Prophylaxis	Group I (<20 yr)	Group II (20-29 yr)	Group III (>30 yr)
No. of patients	17 (10)	18 (9)	27 (20)	25 (15)
Mean age (yr)	18.9	13.3	23.6	39.8
Range	4-36	1-19	20-29	30-62
Days off work/yr	3	4.6	8.8	11.4
Joint pain*	0.6	0.4	1.3	1.6
Joint Bleeds/yr	9.1	14.3	17.0	17.6
Substitution amount (U/kg/yr)	1,927†	1,060	870	720

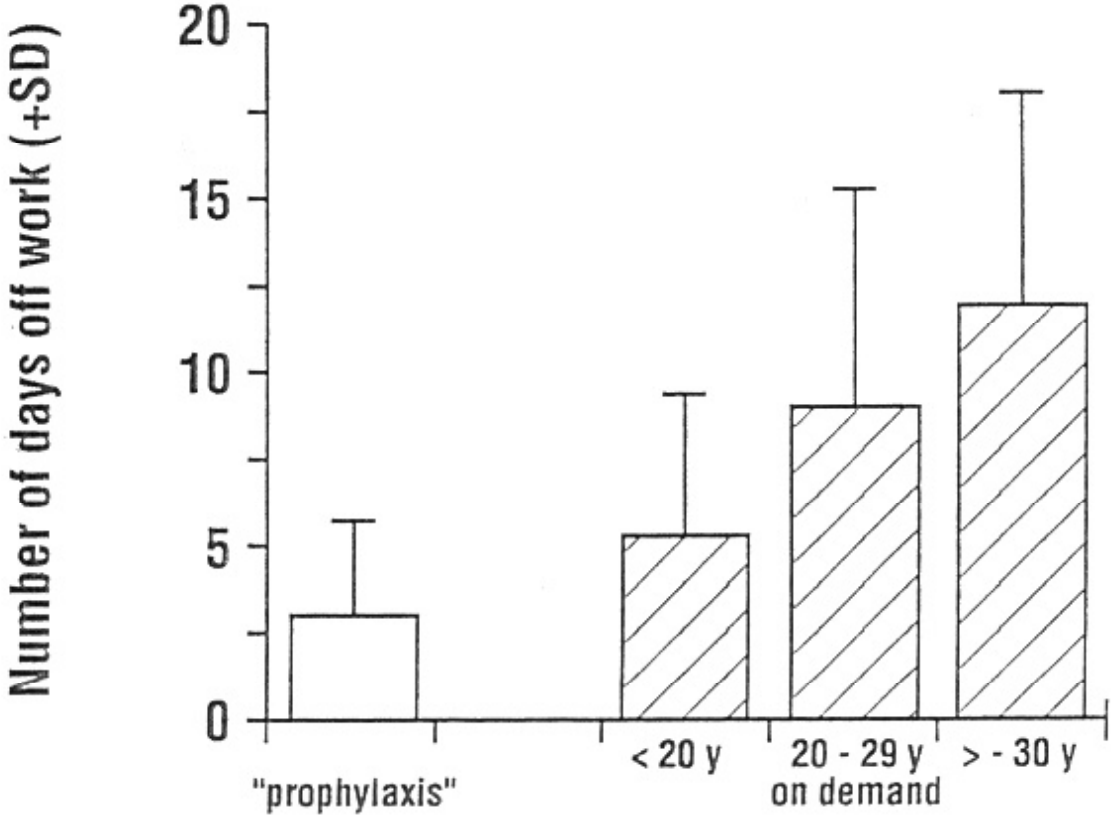
NOTE. The number of pateints available for full radiologic evaluation is shown in parentheses.

*Scale: 0, none; 1, slight; 2, moderate; 3, severe.

†Significant difference ($P < .01$) compared with groups I, II, and III.

Clinical Outcome
Prophylaxis in Haemophilia Treatment

Schramm, W. Experience with prophylactic treatment in Germany.
Royal Society of Medicine Round table series 1991, 25, 12-17.



Haemophilia Care - Outcomes:

Clinical Outcomes and Quality of Life

European Socioeconomic Study
Clinical Outcomes and Resource Utilization Associated with Haemophilia Care in Europe
Schramm W., Royal R., Kroner B. et al, Haemophilia 2002, 8, 33-43

Quality of life differences between prophylactic and on-demand factor replacement therapy in haemophilia patients
Royal R., Schramm W. Berntorp E., et al, Haemophilia 2002, 8, 1-7

Study design: cross-sectional study to collect clinical, economic and quality-of-life data

Centers: 18 treatment centers participated (CCCs)

10 Countries:

Germany	**Italy**	**Netherlands**
England	**France**	**Switzerland**
Sweden	**Greece**	**Israel**
Spanien		

Number of Patients:

Clinical outcomes: n=1005

Quality-of life: n=903

Results - Patients

	Total population n = 1005	On -demand n = 670	Prophylaxis n = 335	p-value
Age				
Mean	34.8	35.4	33.6	0.048
Standard deviation	13.8	13.7	13.9	
Range	11-83	11-82	12-83	
Haemophilia type in %				
Haemophilia A	83.5	83.1	84.1	0.681
Haemophilia B	16.5	16.9	15.9	
Factor (units/kg/year)				
Mean	1.904	1.224	3.208	0.0001
Standard deviation	2.682	2.355	2.790	
Range	0-39.000	0-39.000	7.6-35.412	

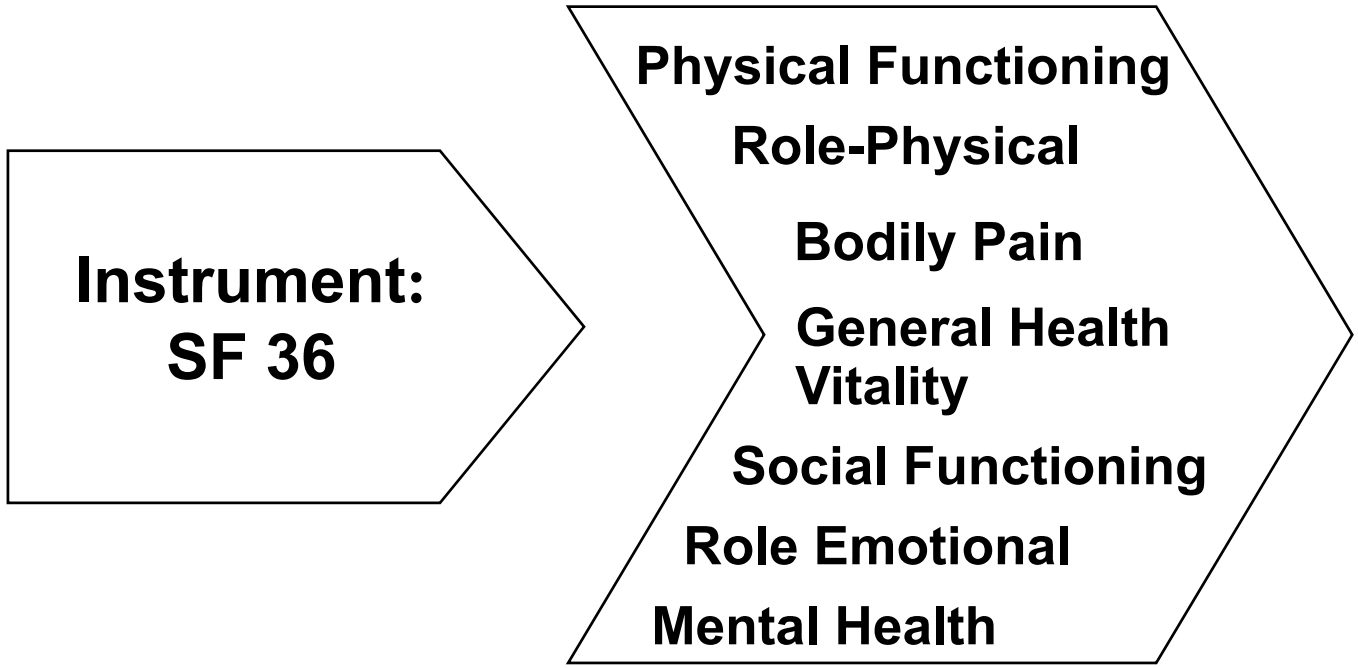
Results - Clinical Outcomes

	Total population n = 1005	On -demand n = 673	Prophylaxis n = 336	p-value
Joint Bleed in %				
Yes	**71.6**	**77.3**	**60.2**	**0.001**
No	**28.4**	**22.7**	**49.8**	
Number of joint bleeds				
Mean number joint bleeds	**6.3**	**7.7**	**3.4**	**0.0001**
Standard deviation	**10**	**11**	**6.3**	
Range	**0-96**	**0-96**	**0-70**	

European Socioeconomic Study
Quality-of-Life

- Number of patients: 903
- Mean age: 35.8
- Objective:
  - Comparison of SF-36 scores in patients treated with factor concentrate proph. and those treated on demand
- Quality-of-life measurement:
  - Medical Outcomes Trust Short Form 36 (SF-36)
  - German population scores were used for comparison

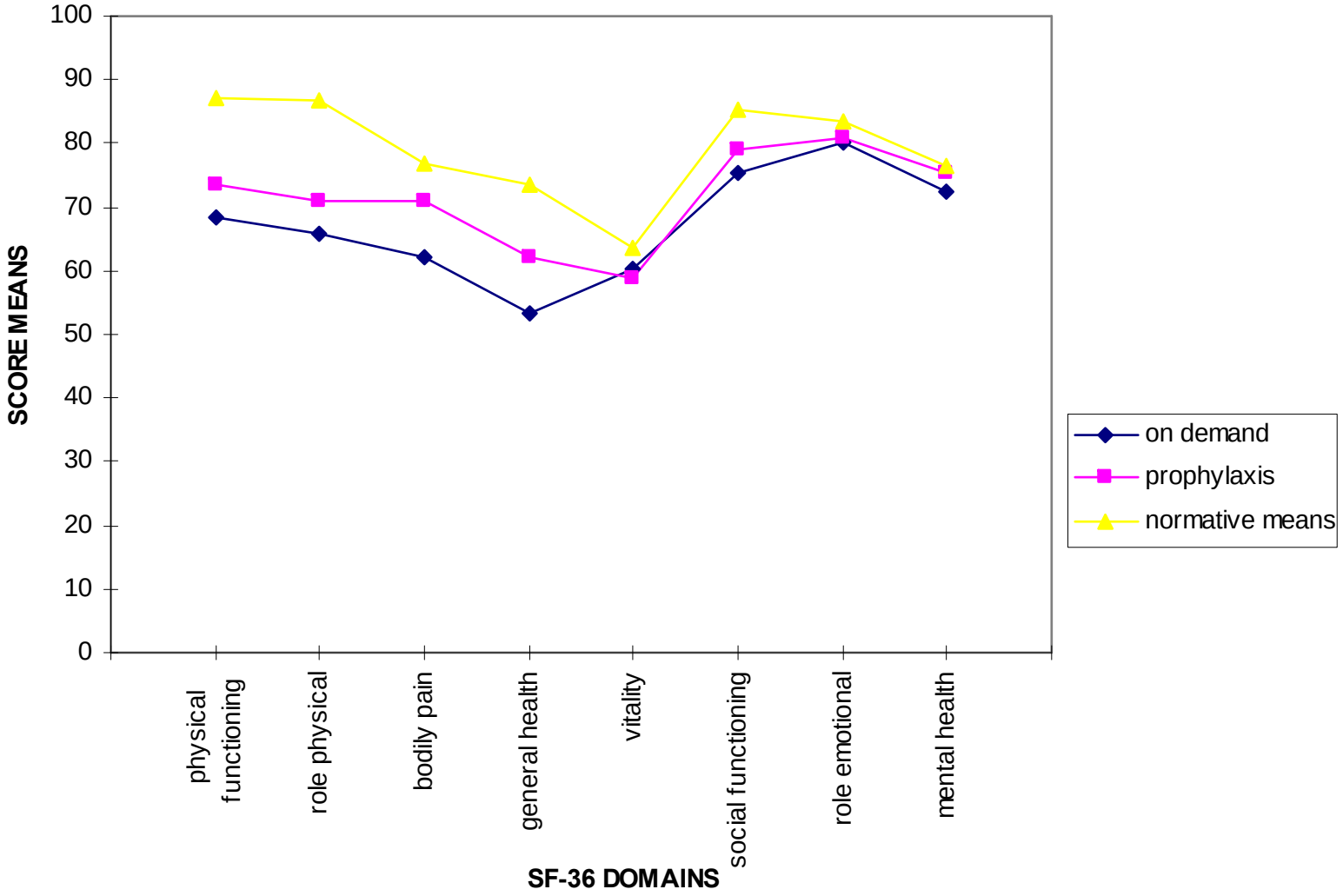
Quality-of-life of Haemophiliacs



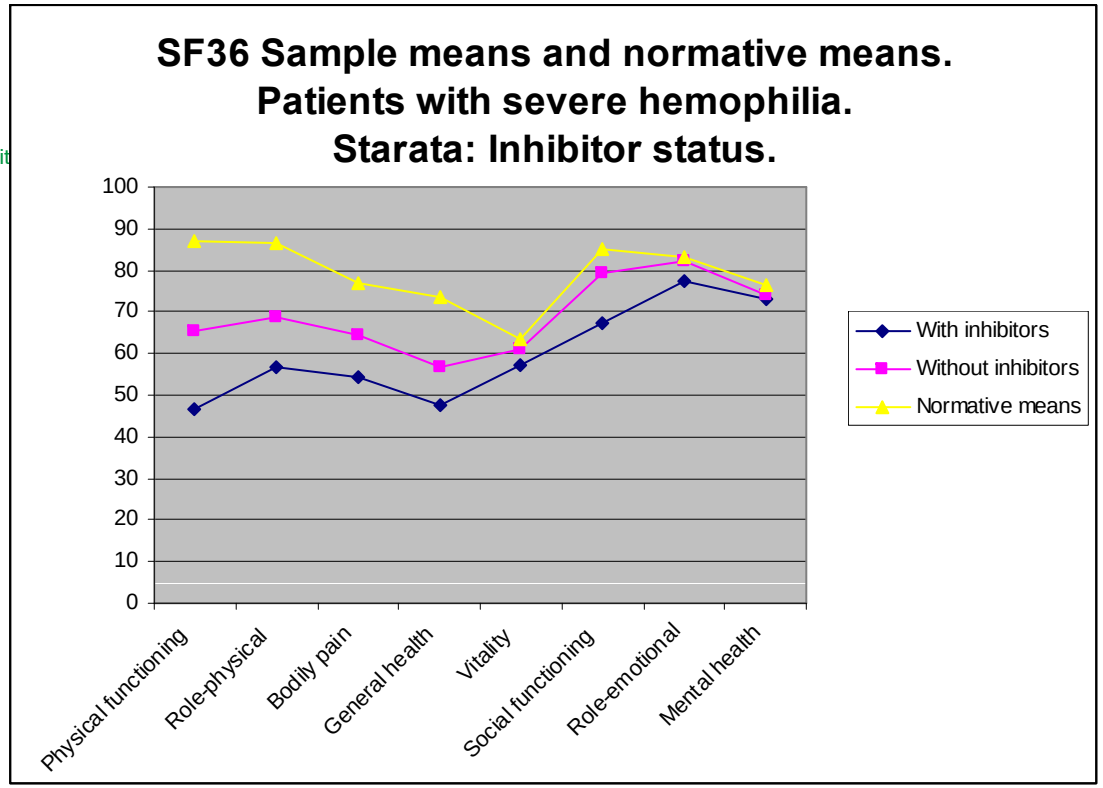
SF-36 Analysis Results for Full Study Cohort

SF-36 Dimension	Mean Score				P value
	On Demand (n=590)	S.E.	Prophylaxis (n=313)	S.E.	
*Physical Functioning	68.40	1.54	73.50	1.95	< .02
Physical Role	65.99	2.52	70.83	3.20	n/s
*Bodily Pain	62.28	1.68	71.01	2.13	< .001
*General Health Index	53.46	1.50	62.12	1.90	<. 001
Vitality	60.19	1.23	58.64	1.56	n/s
Social Functioning	75.39	1.61	79.18	2.04	n/s
Emotion	80.14	2.18	81.05	2.77	n/s
Mental Health	72.43	1.21	75.47	1.55	n/s
Multivariate (MANCOVA) Test					**< .0001**

SF-36 SAMPLE MEANS (CONTROLLED) AND NORMATIVE MEANS



Lebensqualit



Quelle: European Socioeconomic Study, data on file

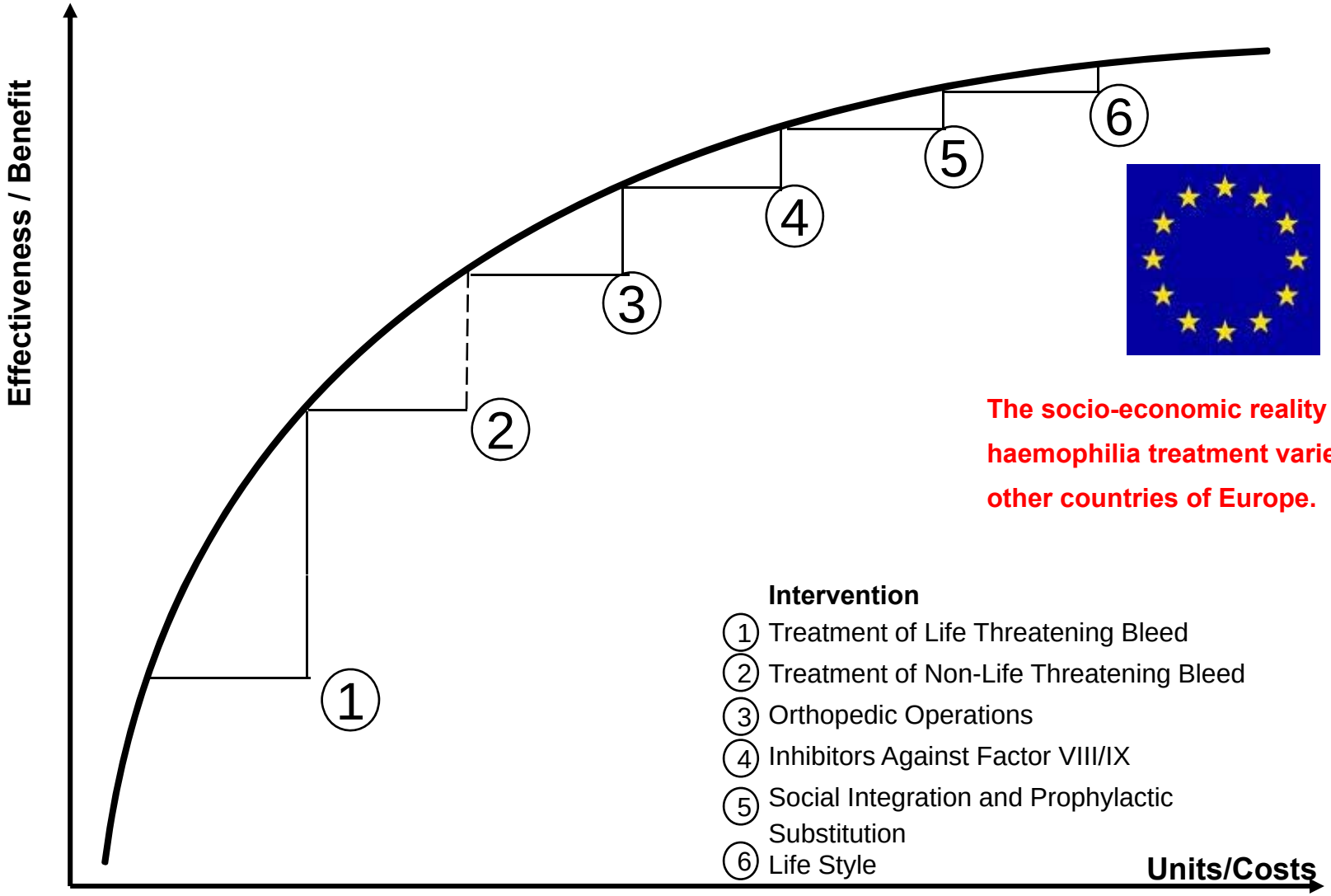
Original study published by
Schramm W et al. 2002 Jan;8(1):44-50.
Royal S et al. 2002 Jan;8(1):44-50

Prophylaxis in Haemophilia Treatment
Open issues

Blood safety in the European Community: An initiative for optimal use.
20-22 May 1999, Wildbad Kreuth, Conclusions: 66

- Time when prophylaxis should start?
- Age at which prophylaxis should be suspended?
- Dosage and frequency of injections ?

Haemophilia Care in Europe

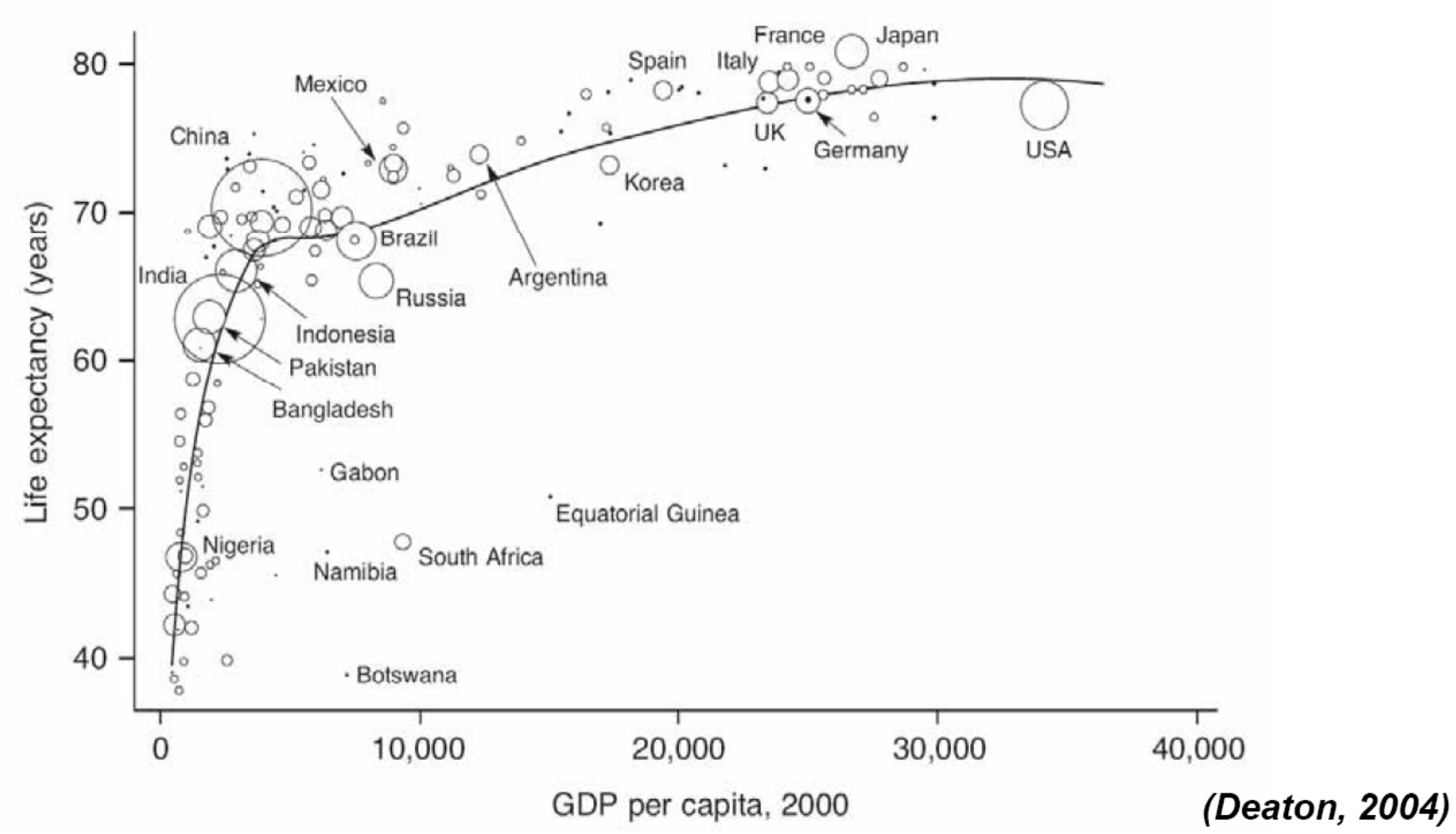


The socio-economic reality and haemophilia treatment varies in the EU & other countries of Europe.

Intervention

1. Treatment of Life Threatening Bleed
2. Treatment of Non-Life Threatening Bleed
3. Orthopedic Operations
4. Inhibitors Against Factor VIII/IX
5. Social Integration and Prophylactic Substitution
6. Life Style

Preston Curve in 2000

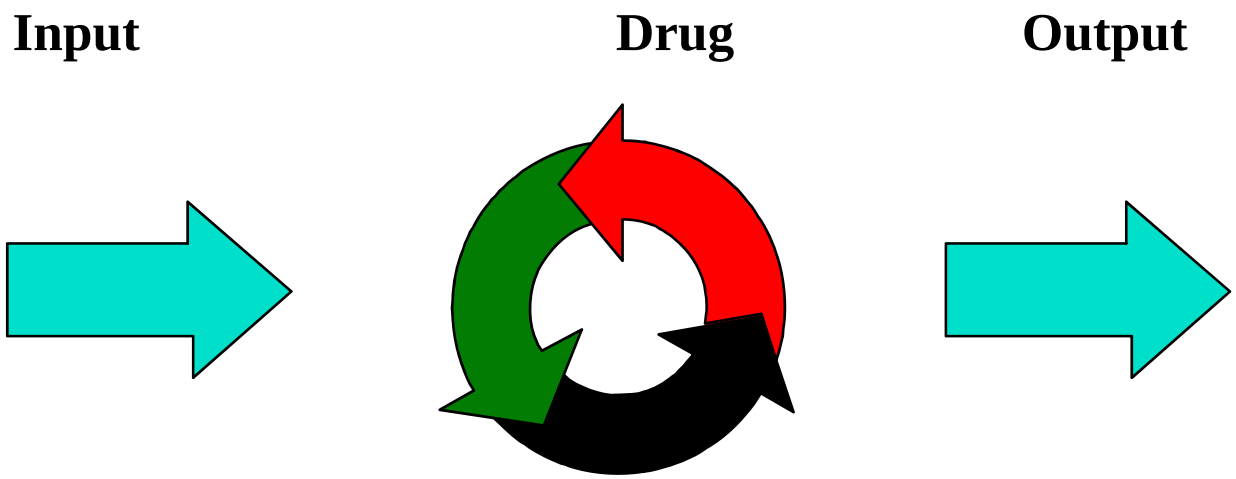


(Deaton, 2004)

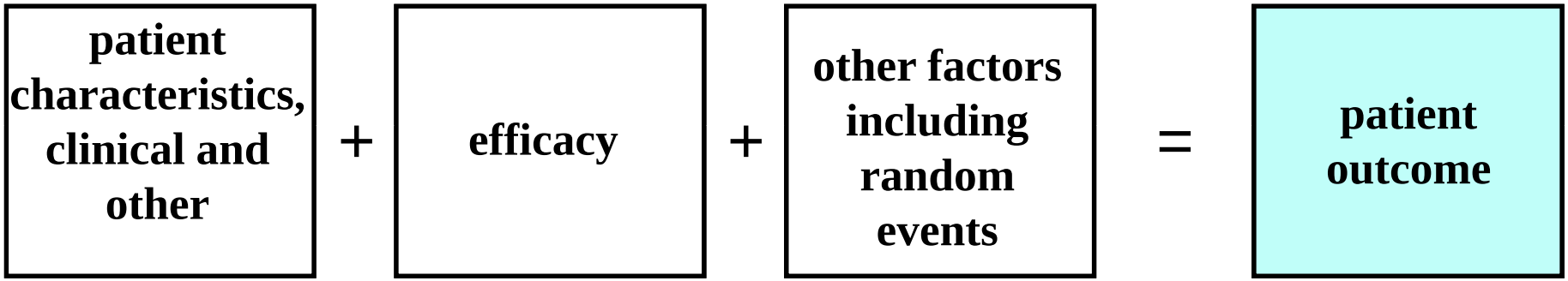
Economic Evaluation of Health Care

A simple economic evaluation of a drug

relates the resources consumed to the output



The “Algebra” of Effectiveness



European **S**tudy of **C**linical, **H**ealth economic and **Q**uality **o**f **L**ife outcomes in Haemophilia treatment (ESCHQoL)

Clinical Outcomes

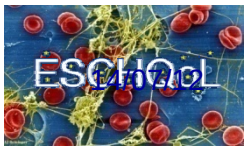
- **Prof. Wolfgang SCHRAMM (coordinator),** UNIVERSITY HOSPITAL OF MUNICH; Dept of Transfusion Medicine and Haemostasis
- **Dr. Paul GIANGRANDE,** OXFORD RADCLIFFE HOSPITALS NHS TRUST, Churchill Hospital
- **Prof. Alessandro GRINGERI,** UNIVERSITY OF MILAN, Dept. of Internal Medicine - Haemophilia and Thrombosis Centre
- **Prof. Rolf LJUNG,** REGION SKANE, UNIVERSITY HOSPITAL, MALMÖ, Paediatrics (Barnkliniken)
- **Dr. Laszlo NEMES**, NATIONAL MEDICAL CENTRE - National Haemophilia Centre
- **Prof. Margit SERBAN**, UNIVERSITY OF MEDICINE & PHARMACY "VICTOR BABES" TIMISOARA – 3rd Paediatric Clinic

Quality-of-Life Outcomes

- **Prof. Monika BULLINGER,** UNIVERSITY HOSPITAL HAMBURG-EPPENDORF OF HAMBURG, Institute and Policlinics of Medical Psychology, Centre of Psychosocial Medicine
- **Dr. Sylvia v. MACKENSEN,** UNIVERSITY HOSPITAL HAMBURG-EPPENDORF OF HAMBURG, Institute and Policlinics of Medical Psychology, Centre of Psychosocial Medicine

Health Economic

- **Karin BERGER**, MSC, MEDICAL ECONOMICS RESEARCH GROUP (MERG) - Munich
- **Dr. Lorenzo G. MANTOVANI,** UNIVERSITY OF MILAN, Centre of Pharmacoeconomics



Funded by: European Commission - DG Research Projekt - QLG7-CT-2002-02475

Objectives – General

- To make available validated instruments for assessment of patients' health status, quality of life and health care and its cost on an European basis
- To identify models of health care of haemophiliacs on the basis of clinical characteristics, their possible costs and impact on quality of life
- To make policy recommendations for optimal care of haemophilia patients on the basis of clinical, quality-of-life and health economic information

Funded by: European Commission - DG Research Projekt - QLG7-CT-2002-02475

Objectives – Clinical Outcomes

- Knowledge about the clinical status and the prevalent treatment modalities in Europe
- Comparison of clinical situations and types of treatment among countries and/or regions of Europe (North, South, East)
- Comparison of clinical status among groups of patients
  - with different age groups (children, adolescents, young adults, older adults and elderly),
  - patients on prophylaxis with patients on ‘on-demand’ treatment,
  - patients prevalently on home treatment with patients prevalently treated at the hospital,
  - patients with inhibitors or patients without inhibitors

Funded by: European Commission - DG Research Projekt - QLG7-CT-2002-02475

Objectives – Quality of Life

- To describe the quality-of life of patients with haemophilia across countries, treatment options and clinical conditions.
- To identify relevant determinants of health related quality-of-life as related to the structure of haemophilia care.
- To compare the quality-of-life outcome of haemophilia care in Europe and recommend future improvements.

Funded by: European Commission - DG Research Projekt - QLG7-CT-2002-02475

Objectives - Economics

- To identify the cost determinants in haemophilia care
- To collect the resource consumption of each of these determinants from the societal perspective and payers perspective (Cost-of-illness analysis)
- To conduct incremental cost-effectiveness analysis and incremental cost-utility analysis
- To describe how CCC are organised in several European countries

Study Design

- Retrospective/prospective, prevalence-based, longitudinal study
- Consecutive patient recruitment will
- Setting: haemophilia comprehensive care centres in 21 European countries:
  - Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Italy, Lithuania, Poland, Portugal, Romania, Slovenia, Slovakia, Spain, Sweden, Switzerland, Turkey, United Kingdom.
- Time horizon
  - Medical Documentation: 12 months
    - Baseline: 6-months retrospective
    - Follow up: 6-months prospective
  - Patient diaries: 6 months prospective

Patients

Patients with mild, moderate and severe haemophilia

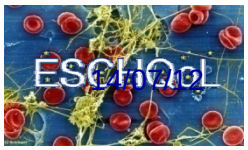
- The severity of clotting factor deficiency was considered according to FVIII or FIX plasma levels as
  - Severe (<1%)
  - Moderate(1-5%)
  - Mild (6-25%)

- Patients with inhibitors were considered according to the anamnestic response to previous exposure to FVIII or FIX as
  - Low responders (<5 Bethesda Units)
  - High responders (>5 Bethesda Units)

Funded by: European Commission - DG Research Projekt - QLG7-CT-2002-02475

Methods
Measurements

Evaluation	Measurement	Informant	Measure Point
Clinical Status	Patients Diary	Patient	Daily
	Medical Documentation	Physician	At enrolment /after 6 months
Health Economic Data	Patients Diary	Patient	Daily
	Patients Preferenences	Patient/Parent	At enrolment
	Haemo-QoL Long/ Short Version	Patient/Parent	At enrolment /after 6 months
	Disease specific questionaire for adults	Patient	At enrolment /after 6 months
	EQ-5D	Patient	At enrolment /after 6 months
Quality of Life	Haemo-QoL Long/ Short Version	Patient/Parent	At enrolment /after 6 months
	Disease specific questionaire for adults	Patient	At enrolment /after 6 months
	SF-36	Patient/Parent	At enrolment /after 6 months
	KINDL	Patient	At enrolment
	EQ-5D	Patient	At enrolment /after 6 months
Desription of Haemophilia CCC's	WHF description of centres questionnaire	Physician/Payers	At enrolment
Additional information	Sociodemographic data	Patient/Parent	At enrolment
	Questions about the disease	Patient/Parent	At enrolment /after 6 months
	Treatment satisfaction	Patient/Parent	At enrolment
	Health care needs	Patient/Parent	After 6 months
	Psychsocial determinants	Patient	At enrolment /after 6 months

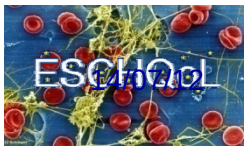


Funded by: European Commission - DG Research Projekt - QLG7-CT-2002-02475

Participation Status

	Clinical Outcome
Number of enrolled patients	1426
Rejection	26
Patients at baseline	1400
Lost for follow up	86
Patients at follow up	1314

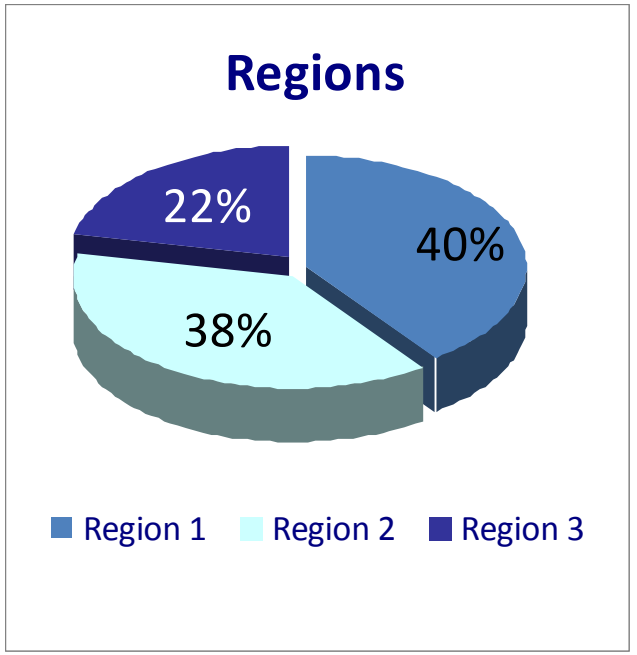
	Patient Diaries
Number of available diaries	1087
Number of diaries with observation time < 150 days	14
Rejection	1
Number of eligible diaries	1072



Funded by: European Commission - DG Research Projekt - QLG7-CT-2002-02475

Results – Clinical Outcomes

- **Region 1 (> 5 IU**): (N=562)
- Austria, Denmark, France, Germany, Sweden, United Kingdom
- **Region 2 (2-5 IU):** (N=540)
- Belgium, Finland, Greece, Hungary, Italy, Portugal, Slovenia, Slovakia, Spain, Switzerland
- **Region 3 (≤ 2 IU):** (N=305)
- Czech Republic, Lithuania, Poland, Romania,Turkey



Definition of regions is based on historical data (2004) from different resources e.g. WFH, market research data

Funded by: European Commission - DG Research Projekt - QLG7-CT-2002-02475

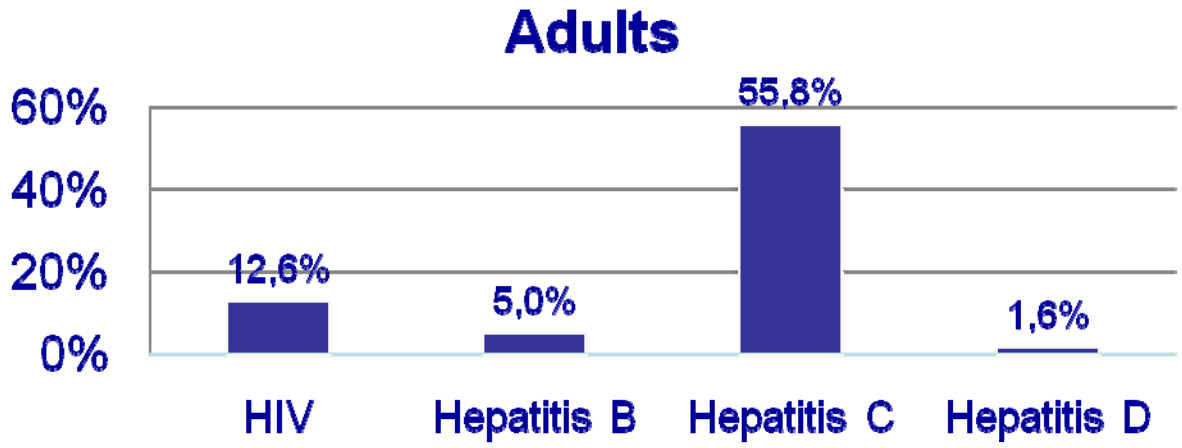
MS3 Zahlen ergeben nicht 1400

MShlaen; 19-02-2009

AC2

Results – Clinical Outcomes
Demographics - Adults

Total	Baseline N=1003	Follow Up N=862
Age (years) Median (Mean +/- SD)	33 (35.3+/-14.4)	32 (34.5+/-14.9)
Height (cm) Median (Mean +/- SD)	176.0 (176.1+/-9.1)	177.0 (176.4+/-8.3)
Weight (kg) Median (Mean +/- SD)	75.0 (75.9+/-14.6)	75.0 (76.1+/-15.0)
Body Mass Index (kg/m²) Median (Mean +/- SD)	24.1 (24.4+/-4.2)	24.0 (24.4+/-4.3)



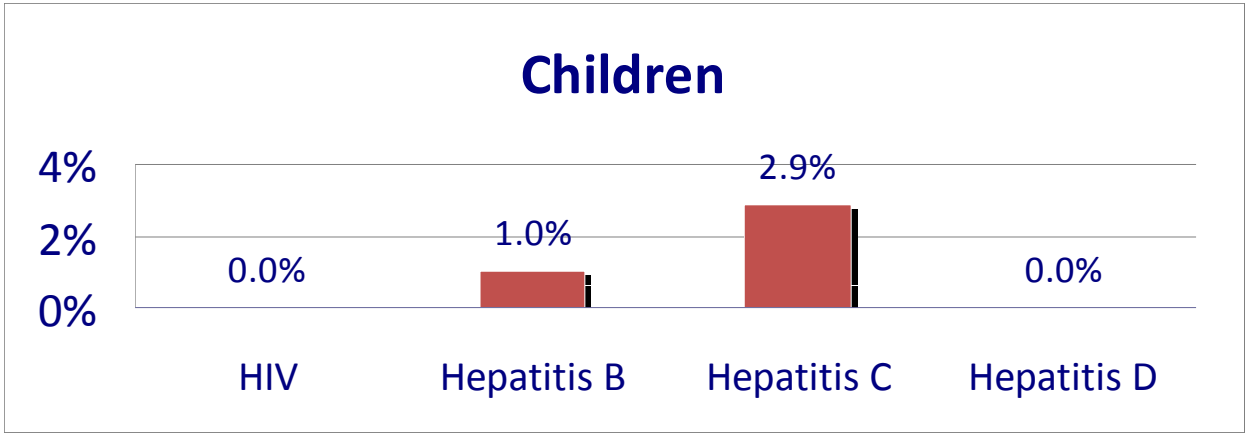
Slide 36

AC2 Auf eine Aufschlüsselung der Komorbiditäten habe ich verzichtet. Die Fallzahlen sind sehr klein, und das Ganze wird schnell unübersichtlich.
Alexander Crispin; 24-02-2009

k3

Results – Clinical Outcomes
Demographics - Children

Total	Baseline N=423	Follow Up N=315
Age (years) Median (Mean +/- SD)	11 (10.7+/-3.4)	11 (11.4+/-3.3)
Height (cm) Median (Mean +/- SD)	148.0 (147.2+/-23.1)	150.0 (150.2+/-21.2)
Weight (kg) Median (Mean +/- SD)	40.0 (43.1+/-23,4)	42.0 (44.5+/-17.7)
Body Mass Index(kg/m²) Median (Mean +/- SD)	17.9 (18.4 +/-4.2)	18.1 (18.8 +/-3.7)

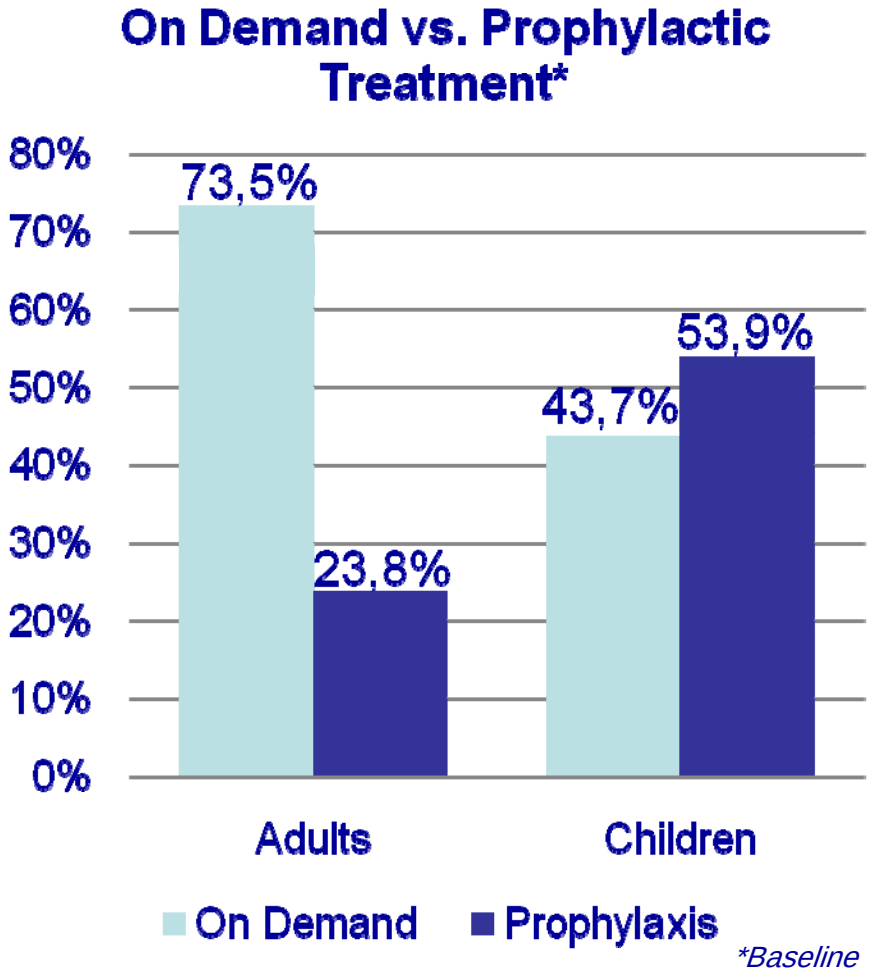


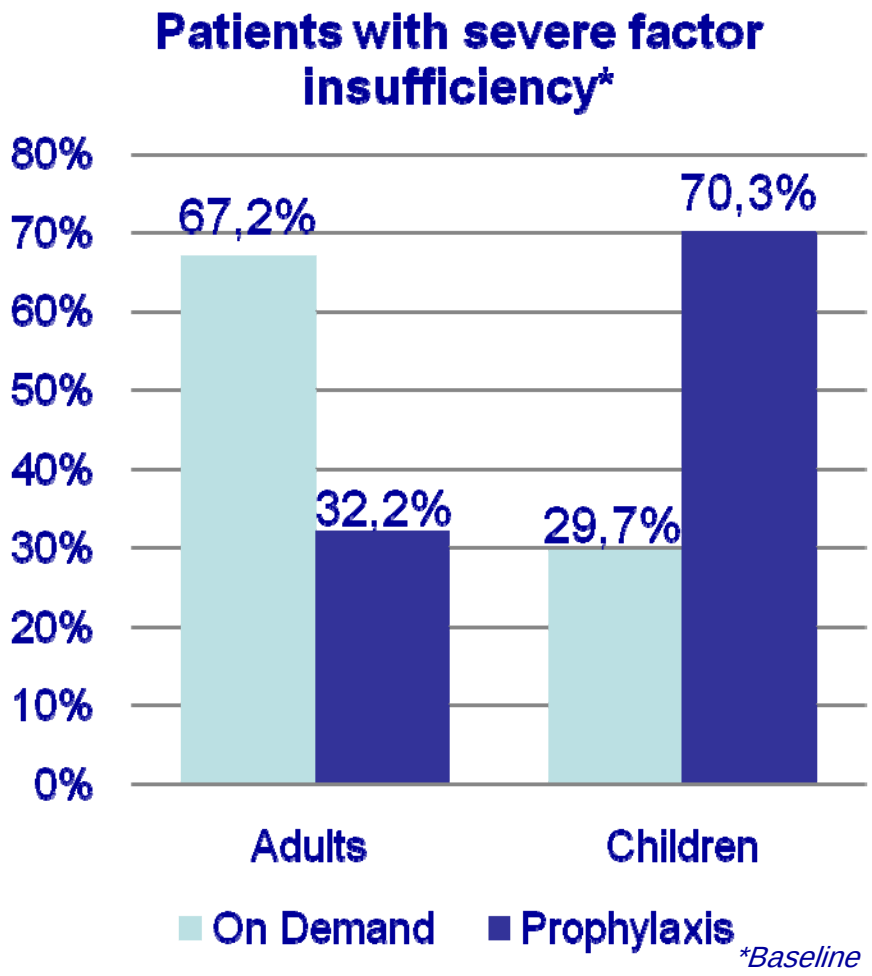
Slide 37

k3 Bitte die Legende kleiner machen

kberger; 22-01-2009

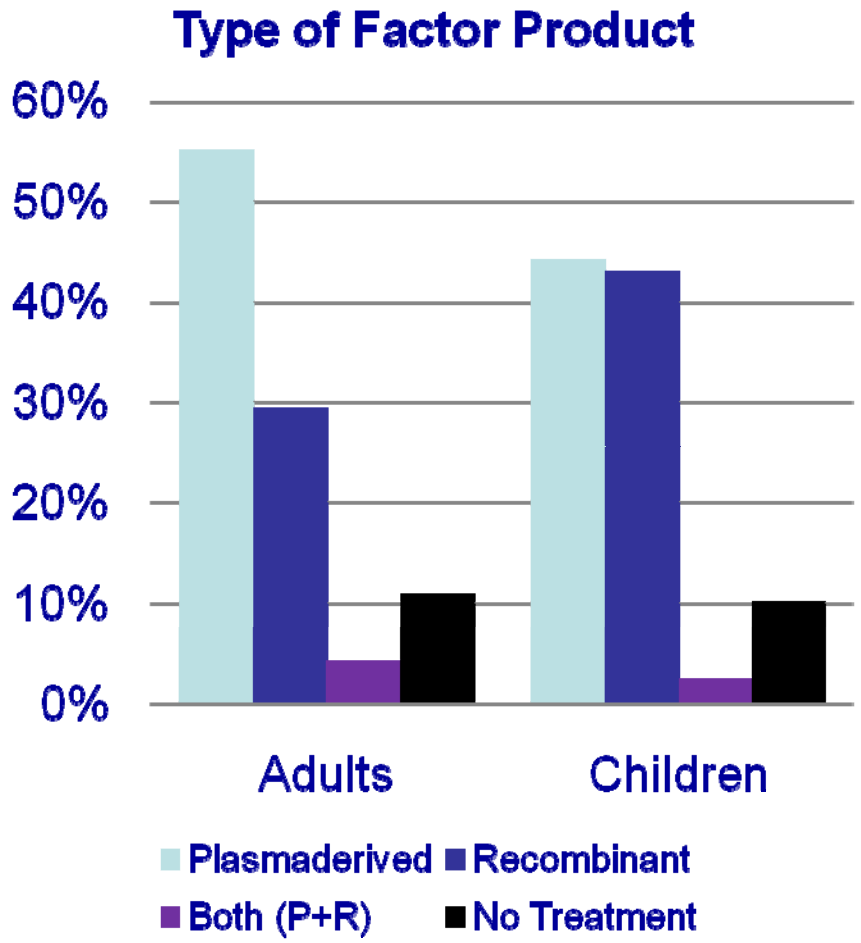
Results – Clinical Outcomes Treatment



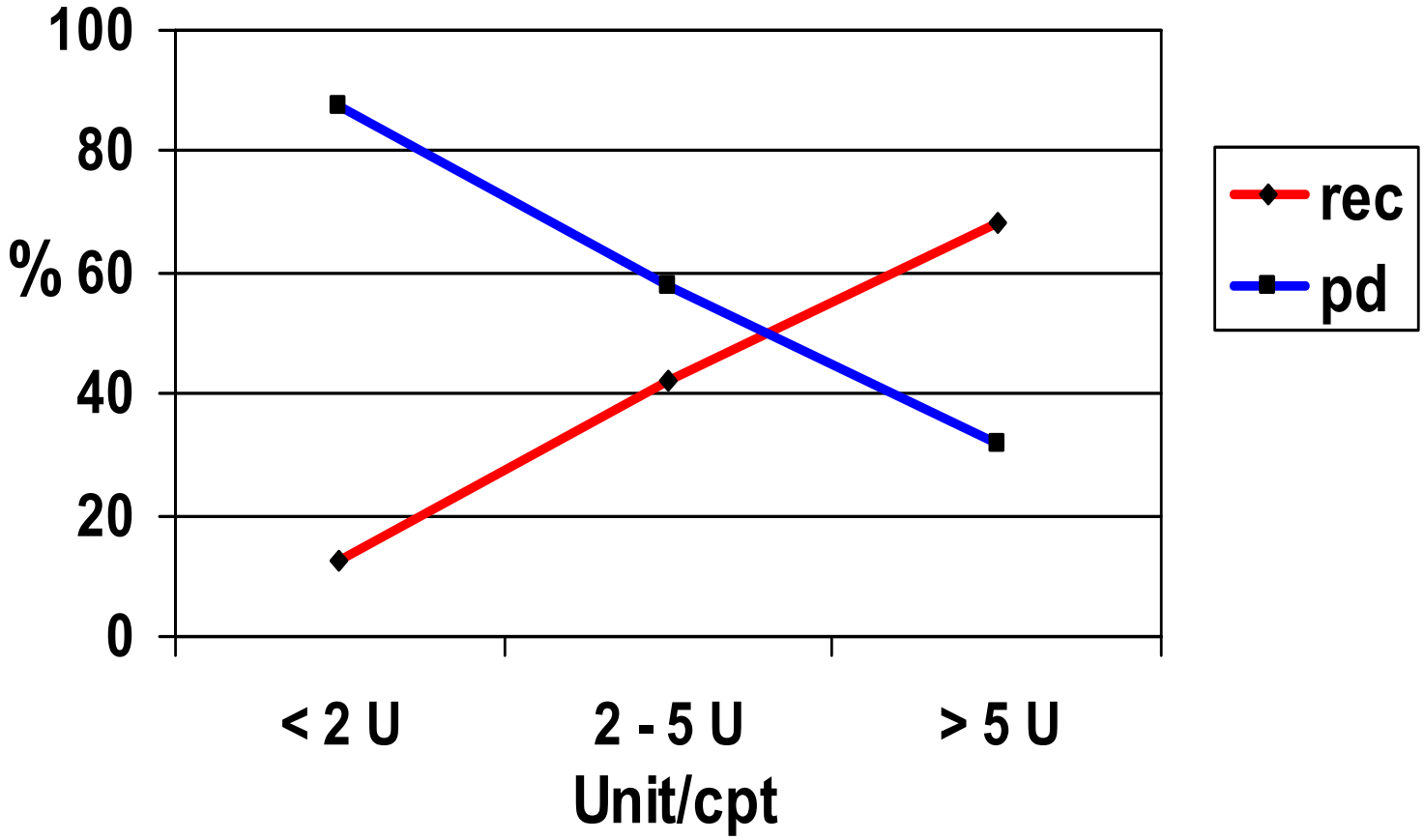


Funded by: European Commission - DG Research Projekt - QLG7-CT-2002-02475

Results – Clinical Outcomes
Treatment



Usage
plasma derived versus recombinant factors



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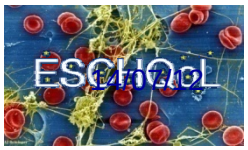
Results Clinical Outcomes
Inhibitors

Inhibitors Adults	Total	Severe	moderate/ mild
Inhibitors history	102 (10,4%)	84 (12,2%)	17 (6,2%)
Inhibitors present N (%)	46 (4.6%)	44 (6.3%)	1 (0.4%)
Age at Inhibitor development (month) Median; Mean (+/-SD)	192; 230.7 (183.8)	168; 205.8 (155.5)	300; 349.5 (259.1)

Inhibitors Children	Total	Severe	moderate/ mild
Inhibitors history	49 (11.8%)	46 (16,7%)	3 (2,2%)
Inhibitors present N (%)	12 (2.8%)	12 (4.3%)	3 (2,2=)0.0
Age at Inhibitor development (month) Median; Mean (+/-SD)	24; 34.9 (32.1)	22,5; 35.0 (32.8)	41; 34.0 (22.3)



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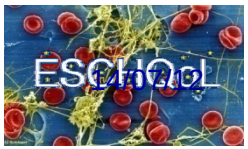
Results – Clinical Outcomes
Bleeding History

Adults	Severe	moderate/mild
Number of bleeds in previous 6 month Median; Mean (+/-SD)	6 10.8 (12.8)	1 4.6 (10.3)
Number of joint bleeds in previous 6 month Median; Mean (+/-SD)	5 9.0 (11.7)	0 4.1 (9.8)
Target joints Median; Mean (+/-SD)	1 1.1 (1.4)	0 0.4 (0.8)
Age at first bleeding (month) Median; Mean (+/-SD)	12 25.8 (36.7)	60 97.7 (123.6)
Age at first joint bleeding (month) Median; Mean (+/-SD)	24 37.2 (41.6)	67 103.8 (115.8)



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Results – Clinical Outcomes
Bleeding History

Children	Severe	moderate/mild
Number of bleeds in previous 6 month Median; Mean (+/-SD)	**3** 4.9 (6.4)	**1** 2.4 (3.9)
Number of joint bleeds in previous 6 month Median; Mean (+/-SD)	**1** 3.1 (5.1)	**0** 1 (2.4)
Target joints Median; Mean (+/-SD)	**0** 0.5 (0.9)	**0** 0.1 (0.3)
Age at first bleeding (month) Median; Mean (+/-SD)	**11** 12.5 (12.4)	**23** 39.2 (41.0)
Age at first joint bleeding (month) Median; Mean (+/-SD)	**18** 24.8 (19.6)	**40** 52.2 (45.7)

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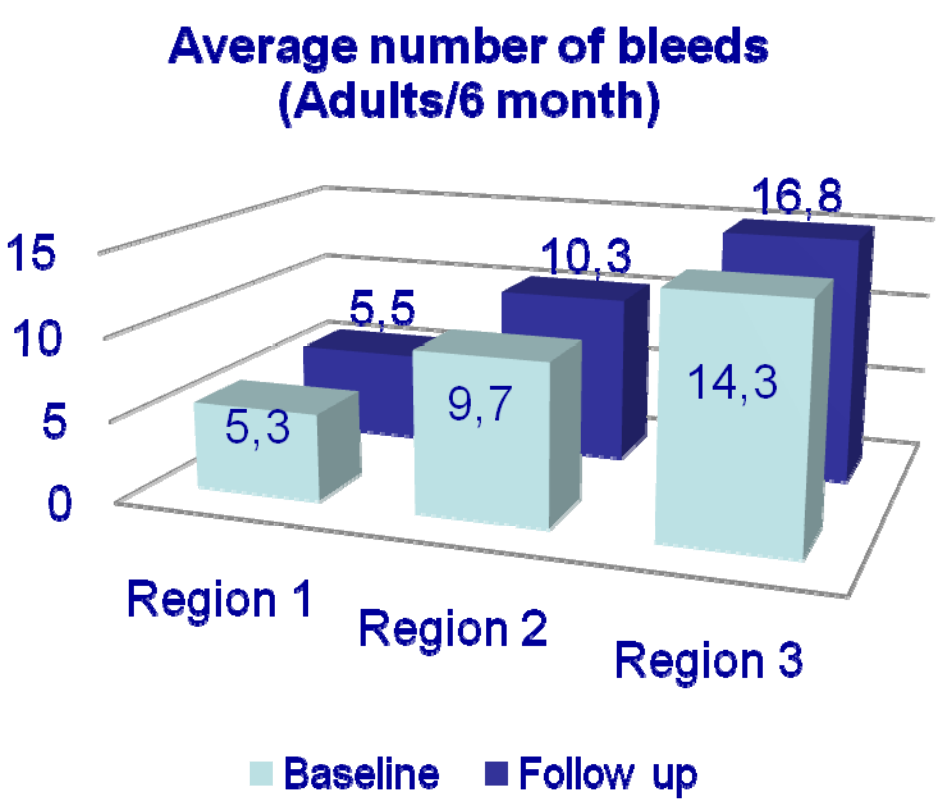
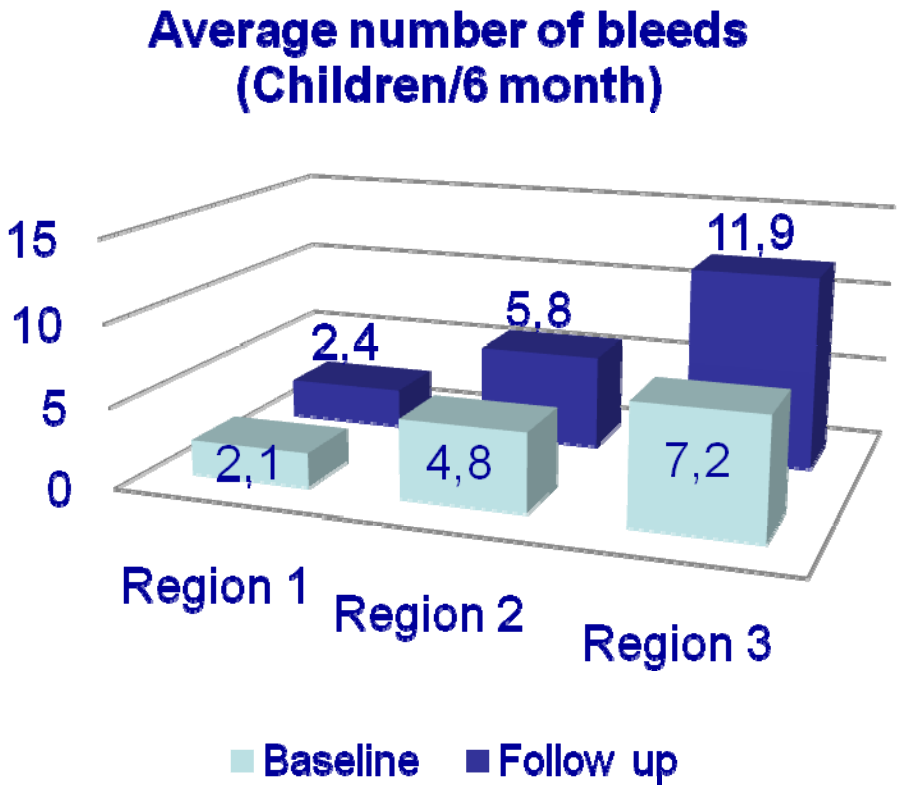
Results – Clinical Outcome
Bleeding History





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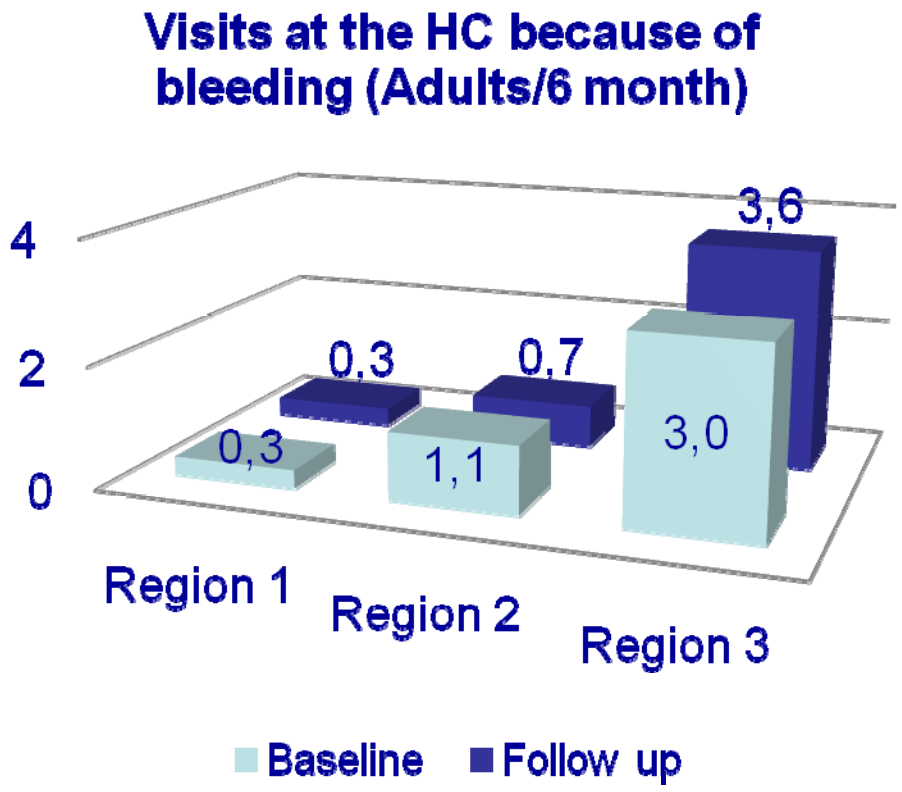
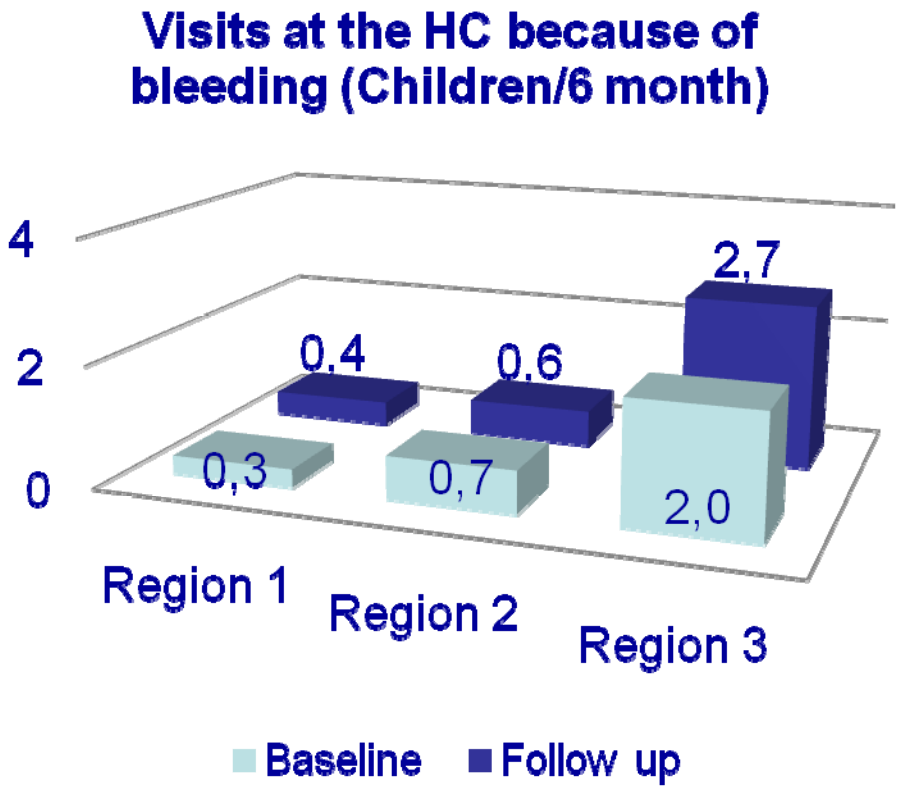
Results – Clinical Outcome
Unscheduled visits at the Haemophilia Center





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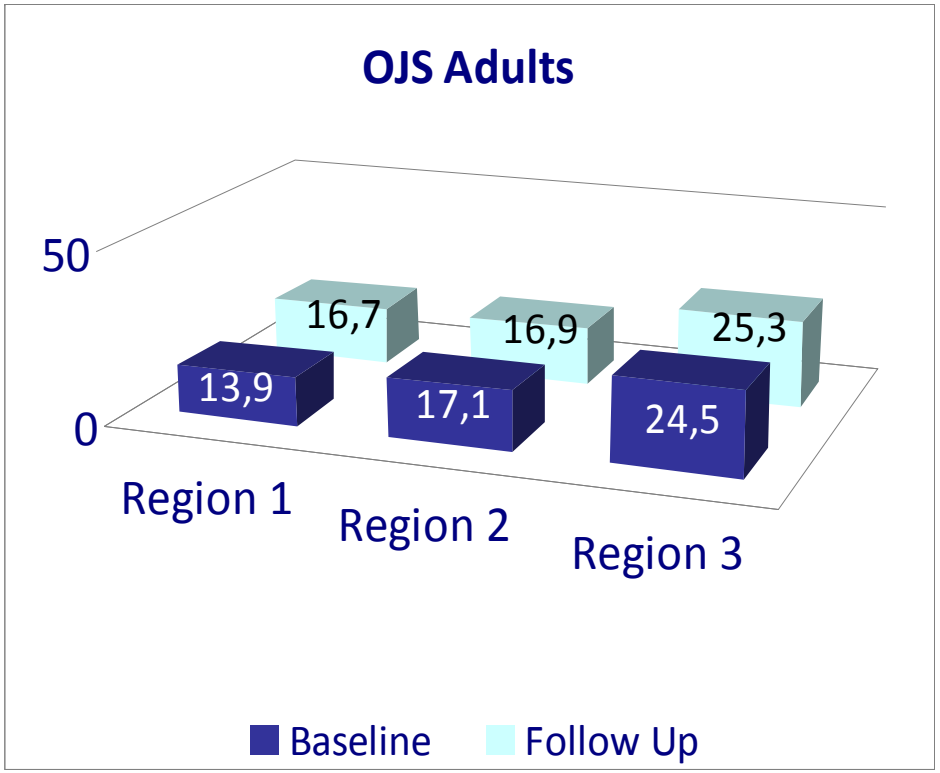
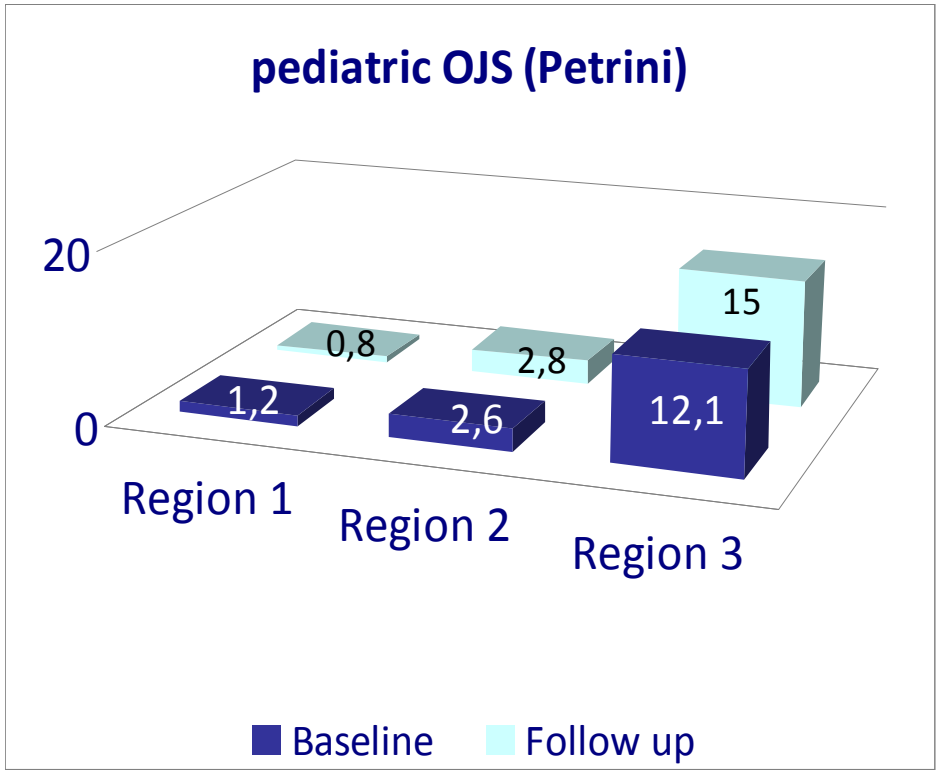
Joint Status II

- The joint scores showed substantial differences between the different regions, especially for children





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Patient's diary

- Every enrolled patient will record on a daily basis for six months any medical event such as
- 'bleeding site',
- 'consultations, examinations, procedures'
- 'therapy administration'
  - occurrence of bleedings,
  - type of replacement therapy,
  - hospitalisations,
  - any kind of medical visits and examinations,
  - school/work days lost by the patients and/or by care-givers).

In order to obtain this information a patient's diary has been prepared, easy to be filled out directly by each patient or guardian.

Patient Diaries

Number of available diaries	1087
Number of diaries with observation time < 30 days	14
Rejection	1
Number of eligible diaries	1072

Results

- Bleeding episodes (days)
- Resource consumption
  - Visit
  - Days lost at work, school or every day live activities
  - Clotting factor use

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MS4

Resource Consumption: Days Lost of Work, School or Every Day Live Activities

	Total (N=1072)			Severe haemophilia (N=761)		
	Patients N (%)	Mean (SD)	Median (Min.-Max.)	Patients N (%)	Mean (SD)	Median (Min.-Max.)
Days lost – patient	439 (41)	13.7 (20.5)	**6.0** (1.0 – 153.0)	344 (45)	15.0 (21.0)	**8.0** (1.0 – 153.0)
Days lost – caregiver	262 (24)	12.6 (21.5)	**5.0** (1.0 – 153.0)	203 (27)	14.3 (23.7)	**5.0** (1.0 – 153.0)

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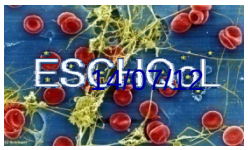
MS4 Sollen die Means raus?

MShlaen; 20-02-2009

Resource Consumption: Clotting Factor Use per Patient Number of Days with Treatment

	Total (N=1072)			Severe haemophilia (N=761)		
	Patients N (%)	Mean (SD)	Median (Min.–Max.)	Patients N (%)	Mean (SD)	Median (Min.–Max.)
Tranexamic acid	95 (8.9%)	24.3 (24.3)	13.0 (1.0 -92.0)	63 (8.3%)	30.7 (26.4)	30.0 (1.0 -92.0)
DDAVP	30 (2.8%)	3.4 (2.3)	2.5 (1.0 -10.0)	13 (1.7%)	2.8 (1.7)	2.0 (1.0 -7.0)
FFP	14 (1.3%)	11.6 (7.4)	10.0 (1.0 -25.0)	13 (1.7%)	12.3 (7.3)	10.0 (1.0 -25.0)
Cryoprecipitate	24 (2.2%)	8.0 (6.4)	5.0 (1.0 -27.0)	23 (3.0%)	8.3 (6.4)	5.0 (1.0 -27.0)
Plasma-derived	557 (52.0%)	32.0 (28.3)	24.0 (1.0 -184.0)	437 (57.4%)	35.2 (29.2)	27.0 (1.0 -184.0)
Recombinant	403 (37.6%)	42.0 (36.0)	34.0 (1.0 -184.0)	322 (42.3%)	46.2 (36.3)	41.0 (1.0 -184.0)



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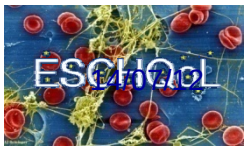
Resource Consumption: Clotting Factor Use per Kg per Year per Patient with Severe Haemophilia

Germany

clotting factor consumption	patients with severe haemophilia		
	N	Mean (SD) IU	Median (Min.–Max.) IU
Plasma-derived and/or Recombinant	147	3,771 (4,304)	**2,932** (40 -43,524)
Plasma-derived	59	3,469 (3,257)	**2,932** (142 -15,068)
Recombinant	93	3,372 (2,401)	**2,732** (40 -9,106)

Romania

clotting factor consumption only	patients with severe haemophilia		
	N	Mean (SD) IU	Median (Min.–Max.) IU
Plasma-derived and/or Recombinant	65	405 (440)	**303** (5 -2,847)
Plasma-derived	44	300 (336)	**223** (8 -1,688)
Recombinant	44	298 (315)	**154** (5 -1,360)



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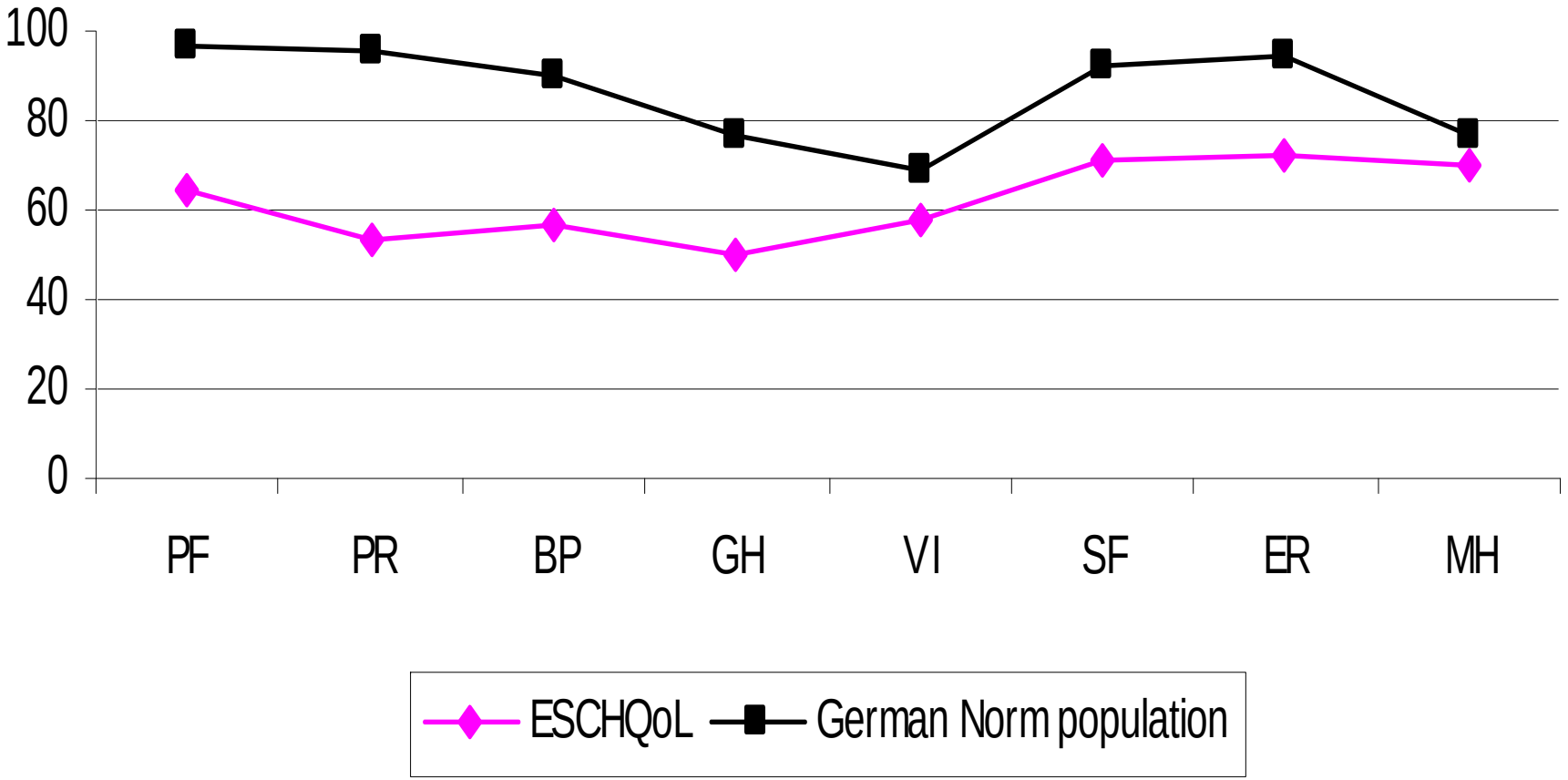
Quality of Life Results

Children and ADULTS

HR-QoL in adults (SF-36) compared to German Norm population



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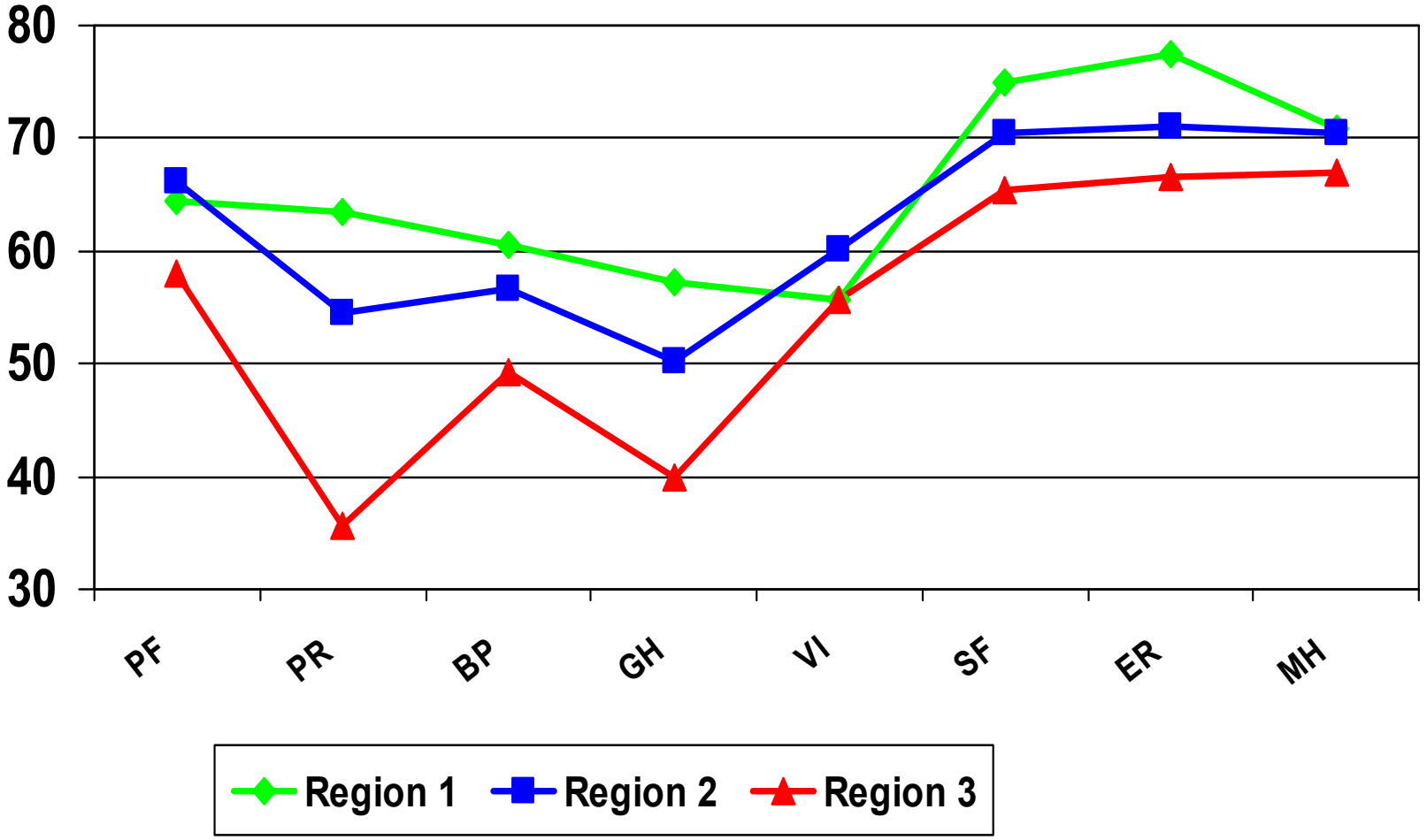
HR-QoL (SF-36) by regions for factor consumption



Why do we need information on Quality of life and patient preferences?