World Haemophilia Day

19 April 2017, Straßbourg

Wildbad-Kreuth Initiative I - IV

EDQM Recommendations

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HAEMOSTASIS AND HAEMOPHILIA

60 YEARS ANNIVERSARY

1938 K. BRINKHOUS: FACTOR VIII

1952 R. BIGGS: HAEMOPHILIA B / CHRISTMAS DISEASE

R. MARX: ACC 76 1.COUMARINANTIDOT (PROTHROMBINCONCENTRAT) TO TREAT **COUMARINBLEEDINGS** !

1953 NOBELPRICE: CITRIC ACID CYCLE / COENZYME A

LITERATURE : WINSTON CHURCHILL

1954 FIRST FACTOR VIII- CONCENTRATE /CRYOPRECIPITAT

1958 I.M. NILSSON: PROPYLACTIC TREATMENT

EARLY 1950: FOUNDATION OF NATIONAL SOCIETIES OF HAEMOPHILIA – UK, CANADA, GERMANY A.O.

50 yrs ago still only a small percentage of haemophilia pts. grew older than 40yrs

Tab. 2. Zur Prognose der *Lebensdauer* von Hämophilen (verschiedenen Schweregrades)

Zeitpunkt	Autor	Prozentsatz der 40 und mehr Jahre alten Personen (abgerundet)
1937	Birch (zit. nach Hecht) (schwere Hämophilie allein ?)	7%
1961	Deutsch	
	a) schwere Fälle (42)	9%
	b) mittlere und milde Fälle (60)	16%
1965	Ahlberg	
	Schwere, mittlere und milde Fälle zusammen (soweit vom Autor selbst untersucht) (157)	18%
1968	Marx	
	a) schwere Fälle (92) – (1961–1968)	10%
	b) mittlere und milde Fälle (68) (1961–1968)	16%
	Deutsch – Ahlberg – Marx zusammen – alle Hämophilie-Typen – (419 casus)	13%
	Bayer. Bevölkerung zwischen 1961 und 1966 (Bayer. Stat. Landesamt)	36–38%

Marx, Prognose der Hämophilien und soziale Probleme, 1968

Challenges in Haemophilia 1953 and 2013

Triple „V“ der Hämophilie

- Verbluten
- Verkrüppeln
- Verarmen

R. Marx 1953

Question of Triple „A“

- Availability
- Access
- Allocation

2013

From Self- Sufficiency to Optimal Use of Blood and Blood Products in Europe – Initiatives from 1989 until 2009

1989

Council Directive of 14 June 1989:
Voluntary unpaid donation
Self-Sufficiency in the EC

1994

EC Communication 1994:

Development and use of quality-assessment criteria and good practices regarding the collection, processing ***and transfusion of blood and blood products and patient follow-up procedures'***
'encouragement of health professionals to make ***optimal use*** of blood and blood products'

1996

1996 Adare, Ireland:
Blood safety and self-sufficiency is influenced by ***„optimal use*** of these products by treating physicians taking fully into account the very special nature of their source".

1998

Vienna 1998:
The ***distribution and transfusion of blood components*** are among the ***final links in the blood transfusion chain.*** They are concerned with both the maintenance of the quality of blood components themselves and the ***quality of the service in delivering and using them.'***

1999

1999 Wildbad Kreuth, Germany:: Rec. No 99

•…transfusion safety should be prioritised on the basis of ***achievable safety gains***.

• **Optimising blood transfusion practices** …in terms of health gain and cost benefit than additional testing strategies.

2007

The EU optimal use project 2007:

The aim of this project is to encourage the optimal use of blood components across Europe through sharing of information

and best practice for the benefit of patients voluntary unpaid donation

2009

European Symposium on „Optimal Clinical Use of Blood Components" April 24th – 25th 2009 Wildbad Kreuth, Germany

Discussion of future challenges

Blood Safety in the European Community – Optimal use of blood components: Wildbad Kreuth Initiatives 1999 - 2016

LMU KLINIKUM DER UNIVERSITÄT MÜNCHEN

Paul-Ehrlich-Institut

edqm European Directorate for the Quality of Medicines & HealthCare

COUNCIL OF EUROPE CONSEIL DE L'EUROPE

Blood Safety in the European Community: WBK I (1999): recommendations/conclusions

OPTIMAL USE IS TO AVOID[1] ...

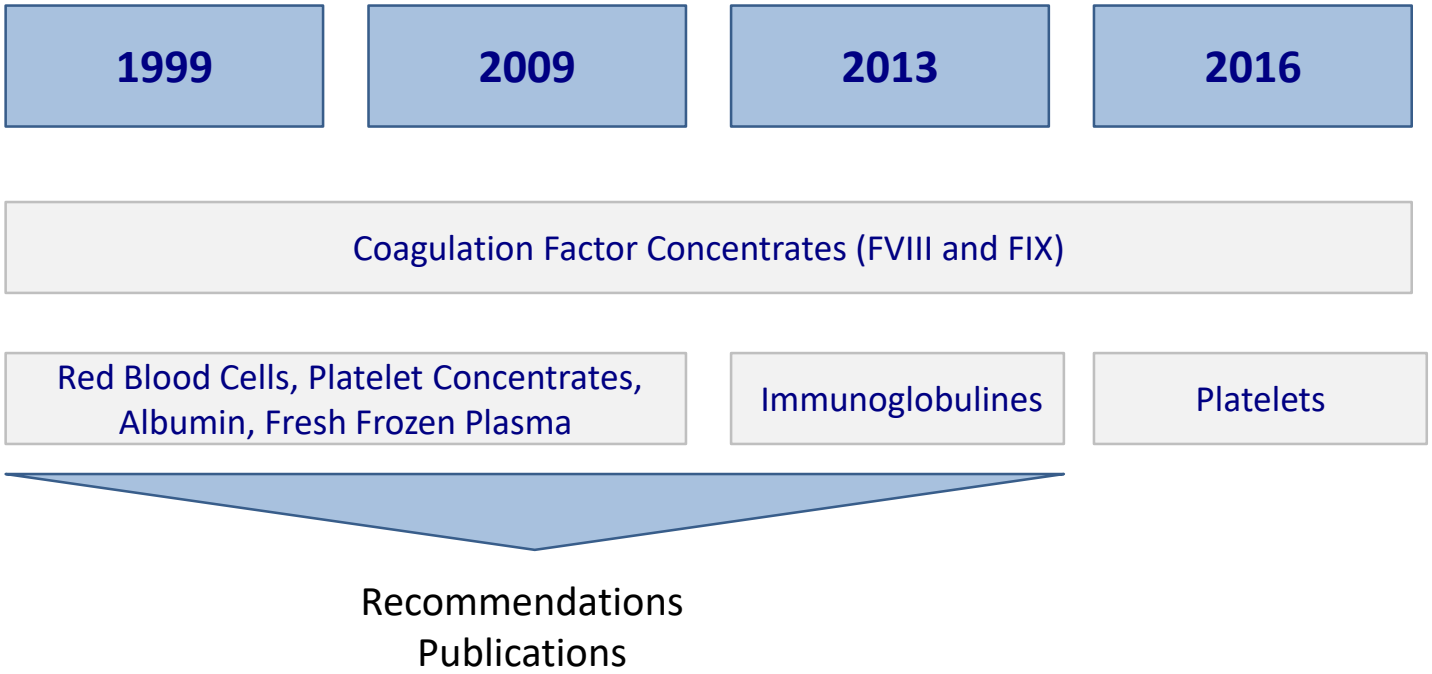
- Overuse
- Underuse
- Inappropriate use

OPTIMAL USE IN HAEMOPHILIA CARE REQUIRES[2] ...

... administering the right quantity of the right blood product in the right way at the right time to the right patient, and appropriate documentation of both the process and the outcome.

[1]Advisory Council on the Assessment of Developments in the Health Care System: Report Appropriateness and Efficiency 2000/2001, Addendum
[2]Wildbad Kreuth Initiative: Conclusions and Recommendations No 71

Optimal Use of Blood and Blood Products in Europe
Wildbad Kreuth Initiatives (WBK) 1999-2016



Kreuth III: European consensus proposals for treatment of haemophilia with coagulation factor concentrates

Haemophilia (2014), **20**, 322–325
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Recommendations

- To optimize the organization of haemophilia care nationally, it is recommended that a formal body be established in each country to include the relevant clinicians, national haemophilia patient organisation, health ministry, paying authority and (if appropriate) regulatory authorities.
- The minimum factor VIII consumption level in a country should be 3 I.U. per capita.
- Decisions on whether to adopt a new product should not be based solely on cost.
- Prophylaxis for children with severe haemophilia is already recognized as the optimum therapy. Ongoing prophylaxis for individual adults should also be provided when required based on clinical decision making by the clinician in consultation with the patient.
- Children with inhibitors who have failed, or who are not suitable for, immune tolerance therapy (ITI) should be offered prophylaxis with bypassing agents.
- Single factor concentrates should be used as therapy wherever possible in patients with rare bleeding disorders.
- Orphan drug designation for a factor concentrate should not be used to hinder the development, licencing and marketing of other products for the same condition which have demonstrably different protein modification or enhancement.

Principles

1. To optimise the organisation of haemophilia care, a system should be established in each member State to allow the implementation of a multidisciplinary approach for the treatment and care of patients (for example by setting up an advisory body including representatives of the relevant clinicians, national haemophilia bodies, patients' organisations, the health ministry, the paying authority, blood establishments and the regulatory authorities or by setting up centres of excellence);
2. **In each member State, the coagulation factor VIII utilisation level should be at least 3 International Units (I.U.) per capita;**
3. Decisions on whether to use a new or an alternative product should be based on evidence of safety and effectiveness and not solely on cost;
4. The evidence of the effectiveness of different treatment regimes should be strengthened. Prophylaxis is currently recognised as the optimum therapy for children with severe haemophilia. Ongoing prophylaxis for adults should be provided, when required based on a clinical decision by the clinician in consultation with the patient;
5. Prophylactic treatment with bypassing agents should be offered to haemophiliac children who have developed inhibitors and in whom immune tolerance induction therapy has failed or was unsuitable;
6. Single coagulation factor concentrates should be used as therapy wherever possible in patients with rare bleeding disorders.

Rationale Kreuth IV: Open questions on the use of coagulation factor concentrates

- Translation of earlier WBK III?
- Best practices in Europe:
  - Prophylaxis in children & adults?
  - Treatment of eldery haemophilia patients?
  - Issues with ITI?
  - Surgery?
- New therapy approaches (e.g. patient tailored / pharmacokinetic, low dose prophylaxis, gene therapy)?
- Access to innovative factor concentrates?
  - Regulatory aspects/requirements
  - HTA aspects / requirements
- How to advance tools for therapy evaluation (e.g. registries)?

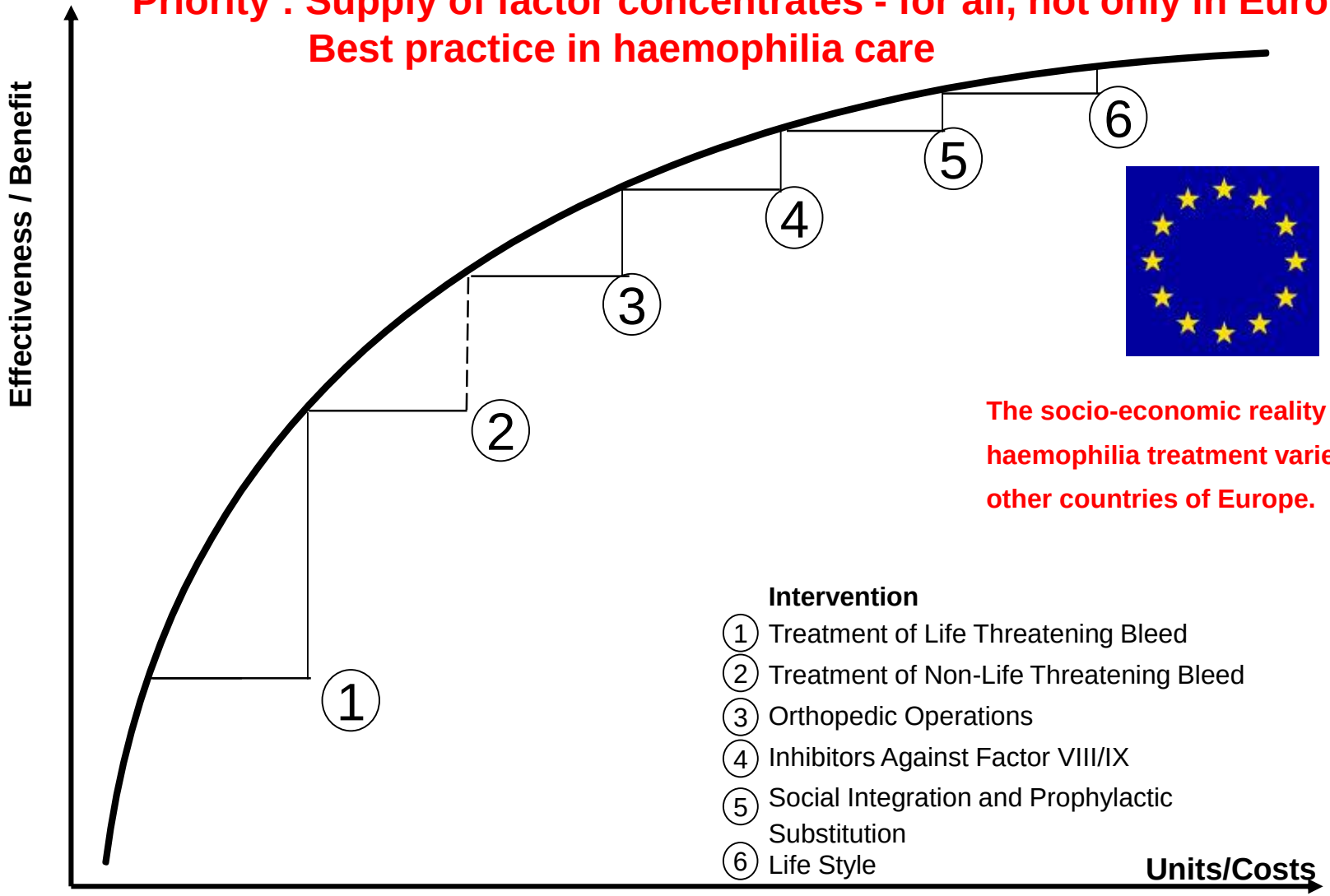
What is the rationale for a number IV WBK initiative with regard to Clotting Factors?

1. **Clotting factors**

- What are the clinical relevance and additional benefit of innovative coagulation factor concentrates?
- How can the results regarding the development of inhibitors with plasma-derived or recombinant clotting factors be seen in clinical practice ?
- How is the progress in the implementation of the WBK III recommendations (resolution CM/Res (2015)3 on principles concerning haemophilia therapies)?
- What are relevant points from the patient perspective?
- How is the development of cost with clotting factors?

Haemophilia Care in Europe

Priority : Supply of factor concentrates - for all, not only in Europe – Best practice in haemophilia care



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

CHALLENGES : YESTERDAY – TODAY – TOMORROW *

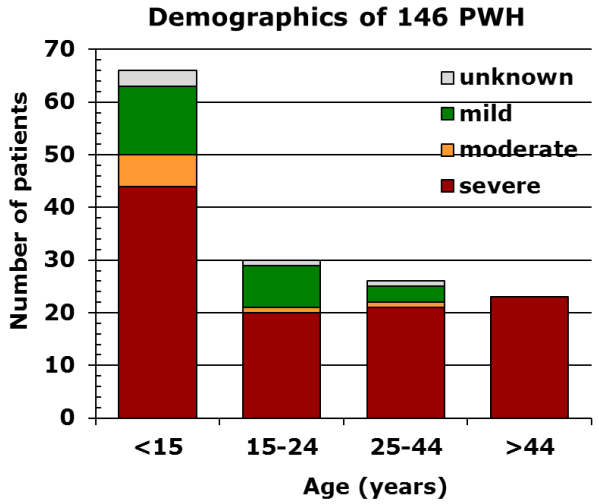
	Yesterday	Today	Tomorrow
Therapy options			
Risk of infection			
Development of inhibitors			
Other adverse events, innovative therapies			
Prophylactic substitution - children			
Prophylactic substitution - adults			
Social integration			
Quality of life			
Supply shortages			
Registries			
Access to innovative therapies			
Compliance, adherence			
Benefit assessment, outcome measurement			
Financing			
Specified methodological standards			

*Karin Berger, Workstream „Outcomes", GTH

SURVEY BY THE BLUTERBETREUUNG BAYERN E.V. (BBB)

YOUR WISHES AS A PATIENT WITH HEMOPHILIA

- Aim: evaluation of unmet medical needs of patients with hemophilia (PWH) in Bavaria from a patient perspective



- Questionnaire of 45 items regarding
  1. Demographics
  2. Therapy, worries related to hemophilia, satisfaction with medical care
  3. Wishes related to extra service and information offers, suggestions how to improve hemophilia care
- Response rate 51.4%

EXAMPLES FROM THE QUESTIONNAIRE

6. Medical care				
	that's right	that's rather right	that's rather not right	that's wrong
1. I am satisfied with the quality of health care				
2. I have confidence in the physicians and the treatment				
3. I am satisfied with the availabi-lity of a physician in charge				
4. Our problems with hemophilia are taken seriously				

9. What would you like to be informed on			
	yes	no	perhaps
1. On general treatment methods / possibilities			
2. On the current state of science			
3. On topics with regard to social legislation like e.g. disadvantageous balancing			
4. On practical everyday helps for the life with hemophilia			
5. On activities for patients with hemophilia			

OFFERS OF THE BBB FOR PSYCHOSOCIAL SUPPORT SEEM TO BE HELPFUL AND NEEDED IN ADDITION TO THE MEDICAL CARE

- **Results**
  - Substitution therapy was mostly uncomplicated
  - Satisfaction with medical care was high
  - „Chronic pain due to hemophilia“ increases in patients >24 years old
  - Overall, 80-100% of patients from all age groups were interested to be informed on the current state of science

- **Conclusions**
  - The survey confirmed the high level of German health care for PWH
  - Most patients wished more information by their treating physicians
  - Worries of elderly PWH and chronic pain should be addressed
  - Offers of the BBB seem to be helpful and needed in all age groups