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Should the same rules be applied to developed and developing countries' plasma for preparation of derivatives?

Albert Farrugia
Vice President Global Access PPTA

THE ANSWER TO THIS QUESTION IS……

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YES !

(Because manufacturing should be geared to clinical relevance and this is identical in all countries)

AND

NO !

- (Because requirements which are irrelevant in developed countries should not be forced onto developing countries
- In fact, such requirements should be removed in all countries
- And relevant requirements considered)

The plasma product paradigm in the developed social market economies

- National blood services funded by government
- Provide transfusion needs – through components
- Embedded in the manufacturing/inventory paradigm
- Driven by RC needs - recovered plasma as a by product
- RP sent for fractionation – generally to a NFP agency
- Aim for self sufficiency – defined as “what's there”
- No or little apheresis production

World Health Assembly 2010

WHA63.12

- *Bearing in mind that treatment using labile blood components is gradually being included in medical practice in developing countries and that thereby* ***increased quantities of recovered plasma should become available for fractionation*** *into plasma-derived medicinal products to meet their needs;*

- *Concerned that in developing countries, blood components separation technology and fractionation capacity are lacking, and that, because of insufficient regulatory controls and failure to implement appropriate practices in blood establishments,* ***plasma from developing countries is often unacceptable for contract fractionation, with considerable wastage of plasma as a result;***

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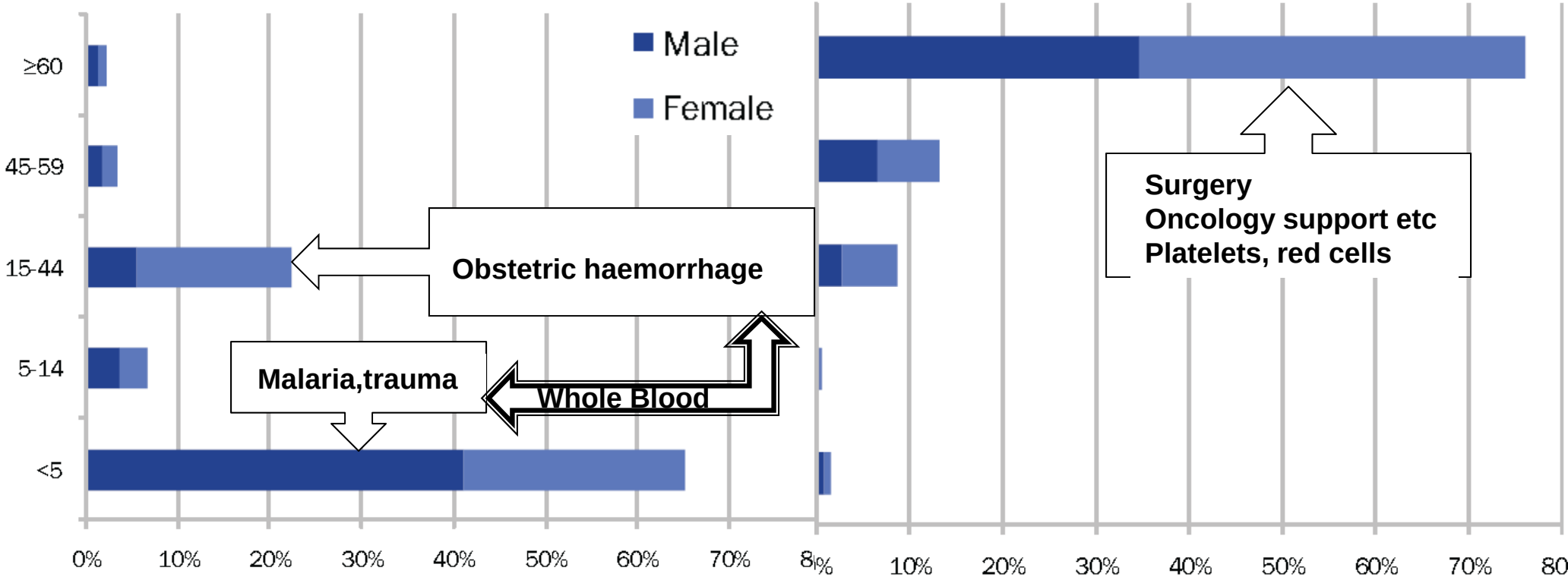
Developing and developed countries
Age and gender distribution of transfused patients



	Benin	Denmark
Population	9099922	5580413
GDP/cap (PPP) $	1481	37151
Transfusions/10^3 population	6.1	9.6

WHO 2011

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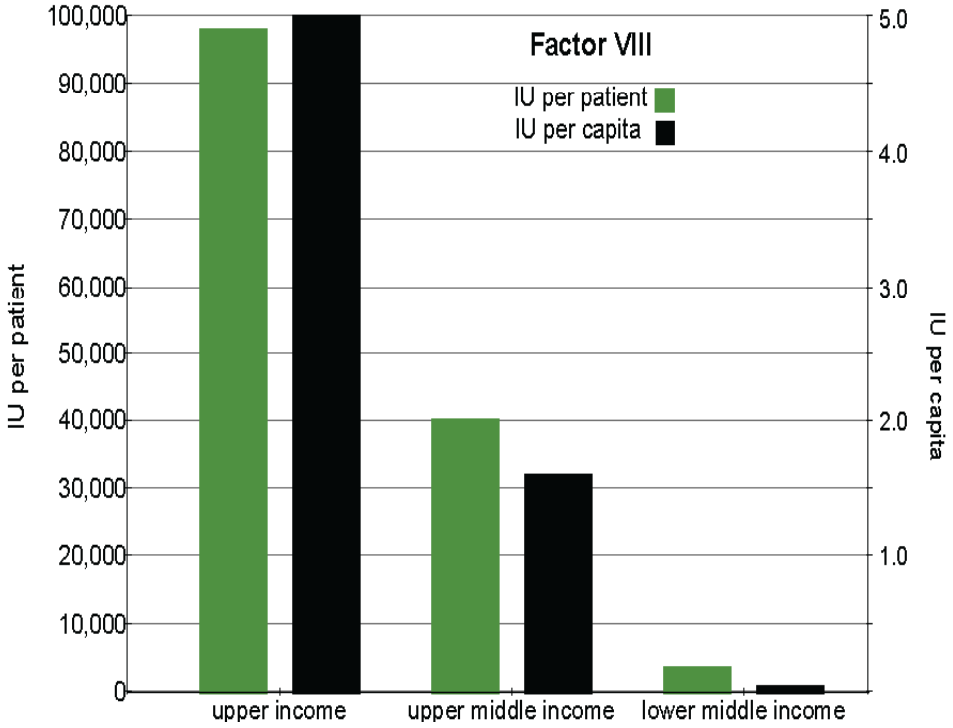
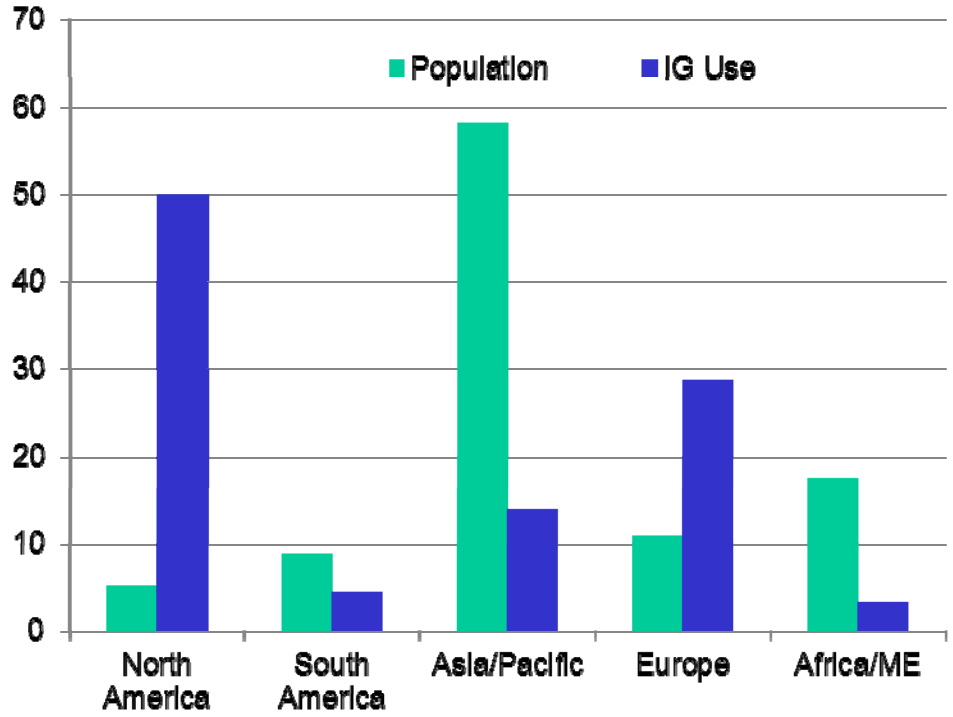
Inequality



WFH Global Survey



Market Research Bureau

Immunoglobulin and FVIII Use in selected countries Political influences

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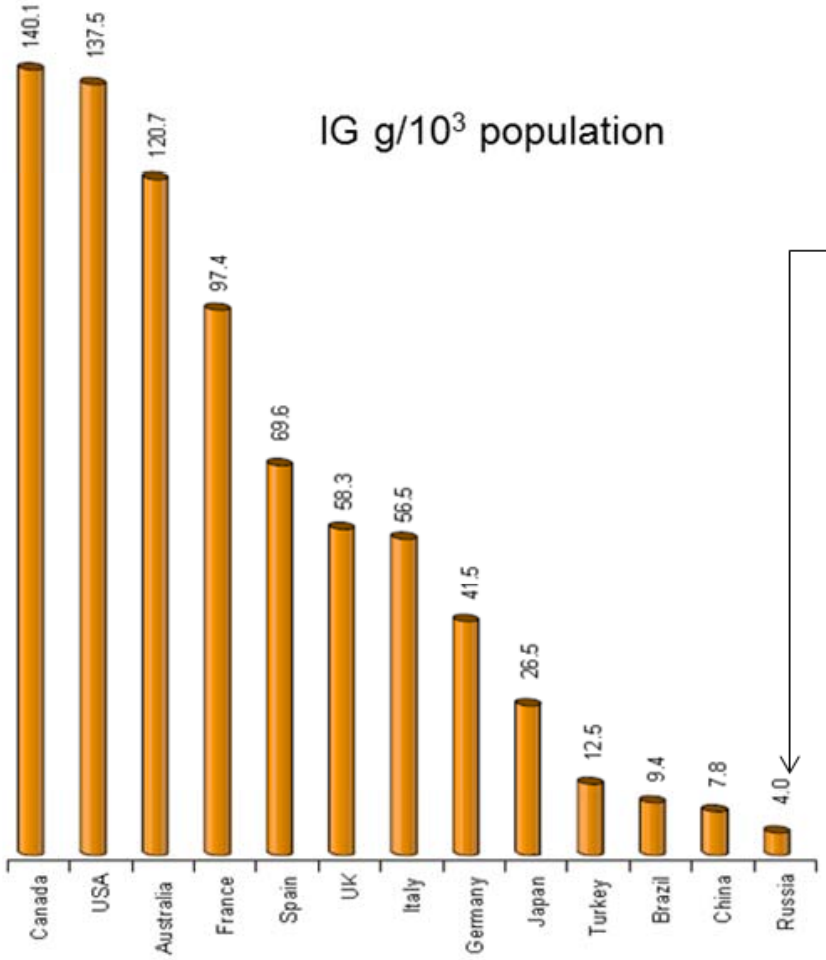

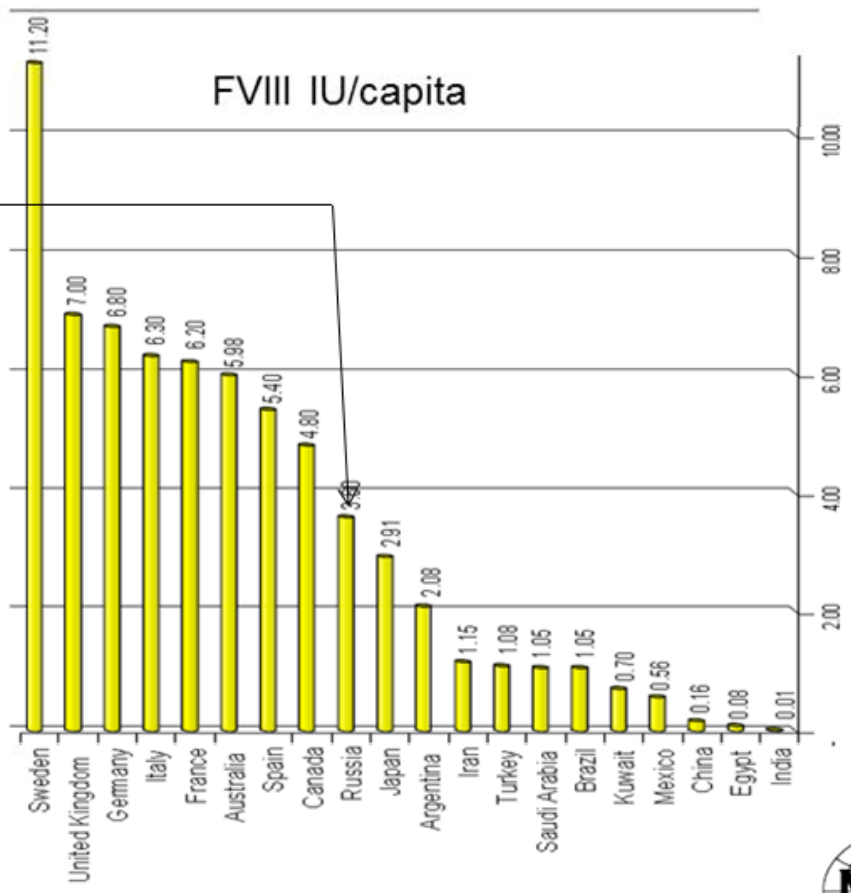

MRB

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Diagnosed prevalence of PIDs
No relation to IG consumption

Country	Prevalence per 10^6 population	IG Kg per 10^6 population
USA	800	138
Australia	280	121
Sweden	150	104
Canada	56	140
India	1	1

Access determines consumption, and is influenced by many factors

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Its not just about resources
Its about priorities !!

- Hungary 55th by GDP, 3rd by haemophilia care
- Ireland 13th by GDP, highest per capita IVIG use in EU
- Japan less Ig/capita than Greece, Portugal,
- Etc etc

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Cryo?

Table II

Risk (%) that a person with hemophilia in Venezuela or U.S.A. will be exposed to HIV-contaminated blood product based on years of treatment and risk of an HIV-infected donation

Years of treatment	Venezuela			U.S.
	Lower (1/25,700)*	Mid (1/21,200)*	Upper (1/17,500)*	Mid (1/545,100)*
5	3.4	4.2	5.0	0.16
10	6.8	8.1	9.8	0.33
15	10.0	12.0	14.3	0.49
20	13.1	15.6	18.6	0.66
30	19.0	22.5	26.6	0.99
40	24.4	28.8	33.7	1.3
50	29.5	34.6	40.2	1.6
60	34.3	39.9	46.0	2.0

* Estimated risk for HIV-infected donation.

"Cryo is evil"

Evatt, Miami, November 02

"… a person with hemophilia who receives monthly infusions of cryoprecipitate prepared from plasma of 15 donors over a lifetime of treatment (60 years) is at significant risk of being exposed to HIV. …in Venezuela, the percentage of risk is 40%...."

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Cryo!

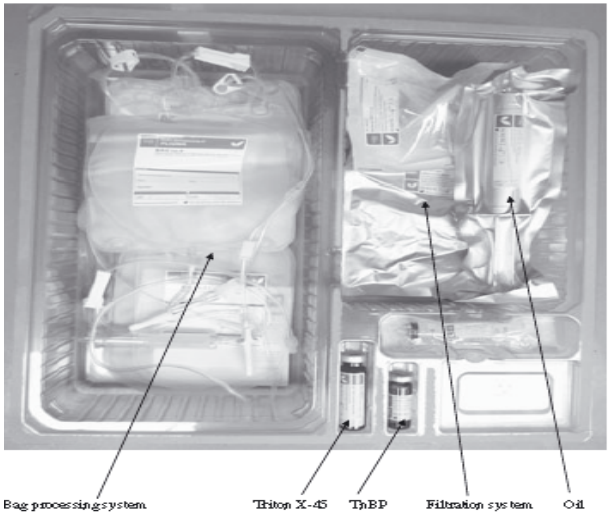
Transfusion Medicine, 2010, **20**, 48–61 doi: 10.1111/j.1365-3148.2009.00963.x

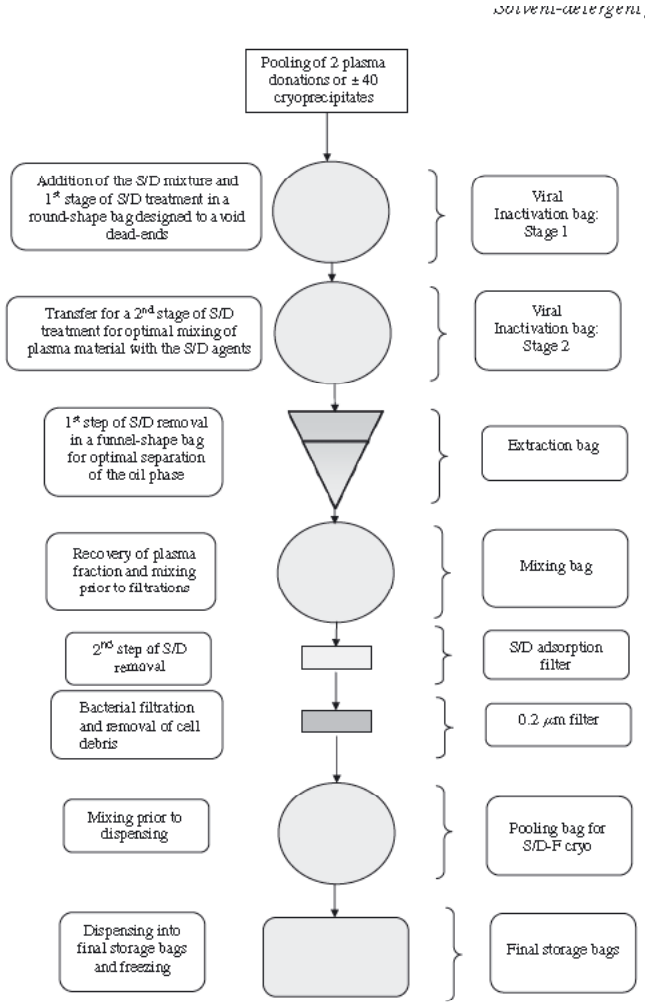
ORIGINAL ARTICLE

Solvent-detergent filtered (S/D-F) fresh frozen plasma and cryoprecipitate minipools prepared in a newly designed integral disposable processing bag system

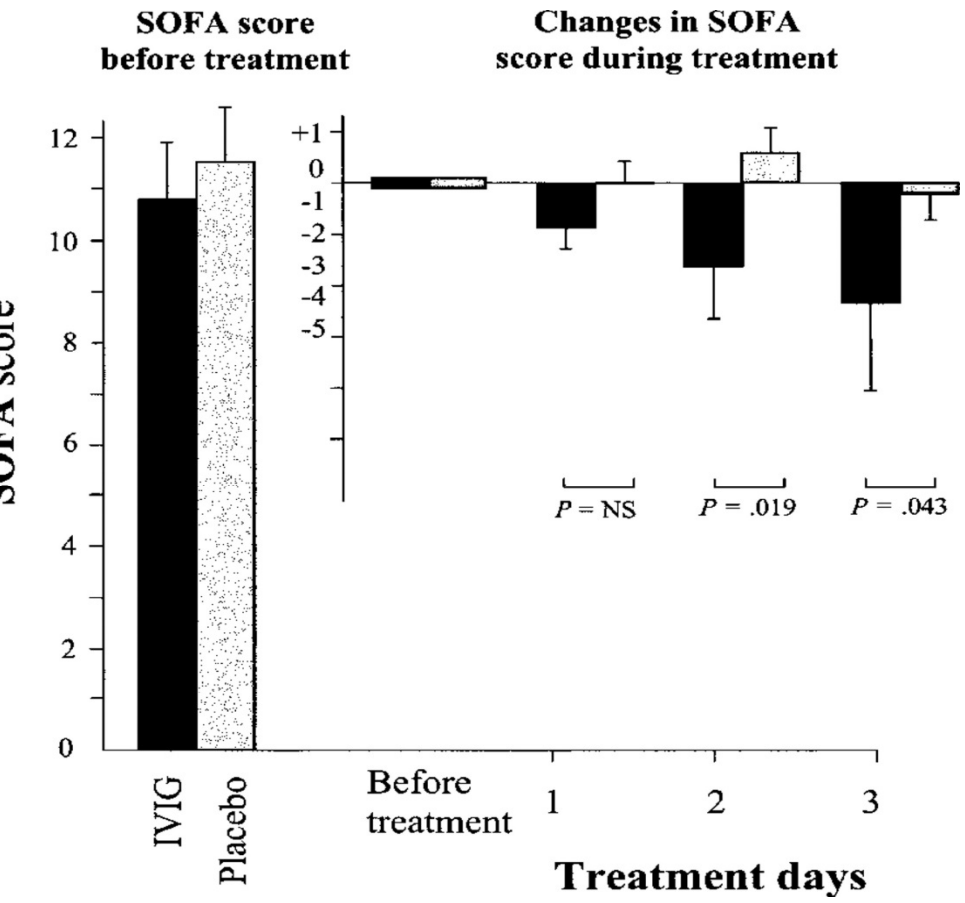
M. El-Ekiaby,[1] M. A. Sayed,[2] C. Caron,[3] S. Burnouf,[4,5] N. El-Sharkawy,[7] H. Goubran,[8] M. Radosevich,[6] J. Goudemand,[3] D. Blum,[4,5] L. de Melo,[9] V. Soulié,[9] J. Adam[9] & T. Burnouf[6]

[1]Shabrawishi Hospital Blood Bank, Giza, Egypt, [2]Fayoum University, Fayoum, Egypt, [3]Laboratoire d'hématologie, Hôpital Régional et Universitaire Lille, [4]INSERM, U837, [5]Université Lille-Nord de France, IMPRT, Jean-Pierre Aubert Research Centre, [6]Human Protein Process Sciences, Lille, France, [7]National Cancer Institute, [8]Faculty of Medicine, Cairo University, Cairo, Egypt, and [9]V.I.P.S. SA Virus Inactivation of Plasma Systems, 2013 Colombier, Switzerland





Intravenous Immunoglobulin G Therapy in Streptococcal Toxic Shock Syndrome



End point	All included patients: IVIG group (n = 10)	All included patients: Placebo group (n = 11)
Primary: mortality day 28, no. (%) of patients	1 (10)	4 (36)
Secondary		
Time to resolution of shock,[a] h		
Mean	88	122
Median (range)	96 (2–159)	108 (47–294)
Time to no further progression of NF/cellulitis, h		
Mean	68[b]	36[c]
Median (range)	20 (2–168)[b]	24 (19–72)[c]
Mortality day 180, no. (%) of patients	2 (20)	4 (36)

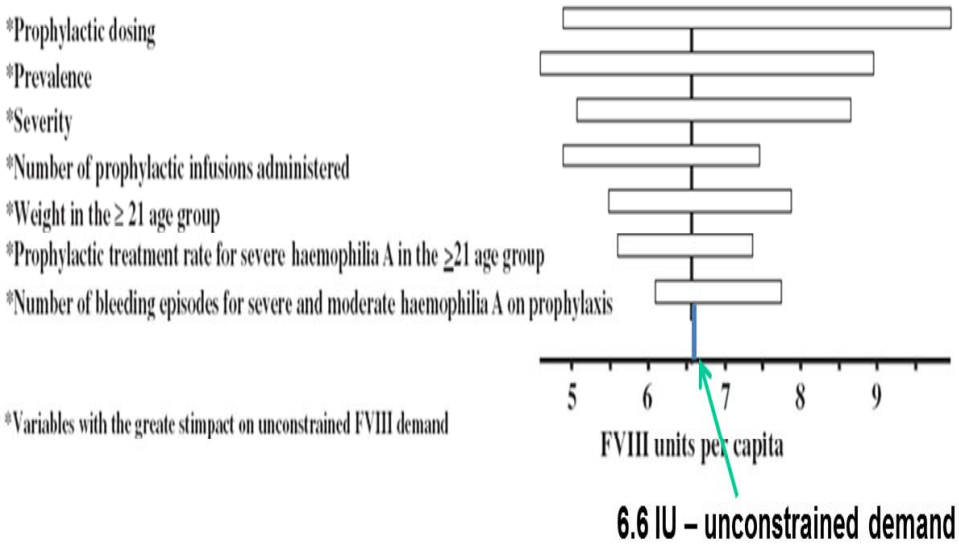
NOTE. GAS, group A streptococci; IVIG, intravenous IgG; NF, necrotizing fasciitis.

[a] In the survivors.
[b] Seven patients.
[c] Five patients.

Darenberg J et al. Clin Infect Dis. 2003;37:333-340

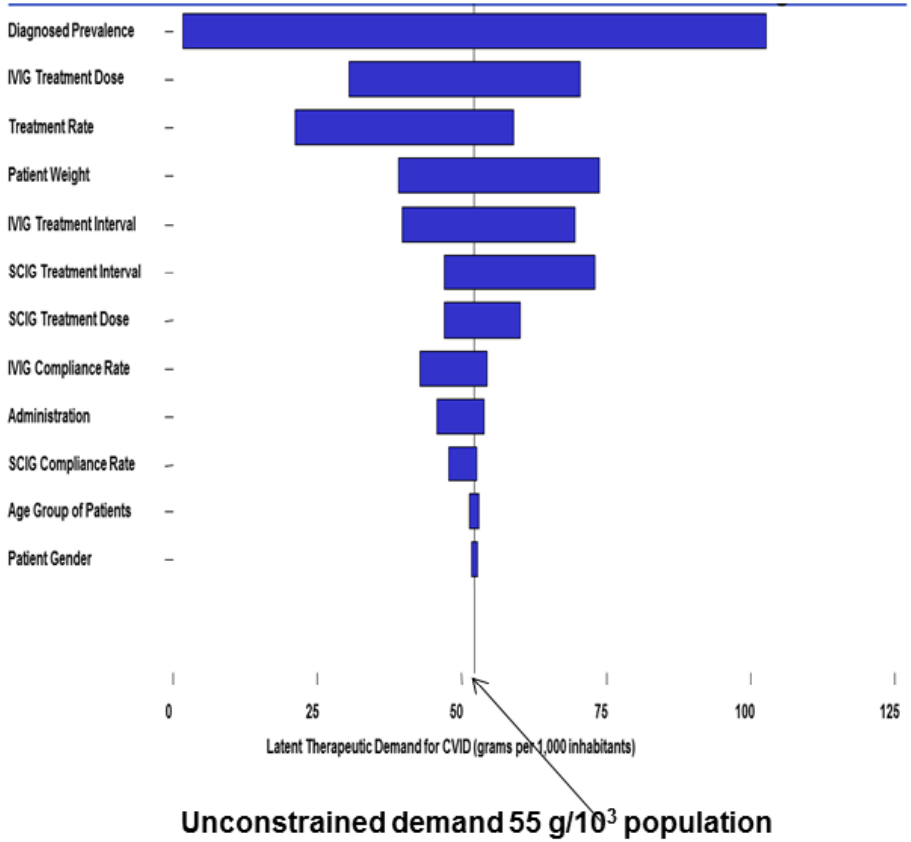
LTD for FVIII in Haemophilia A and IGG in CVID
Decision analysis modeling

FVIII in Haemophilia A



Haemophilia (2004), 10, 18–26

IGG in CVID



Proc ESID 2012 *in press*

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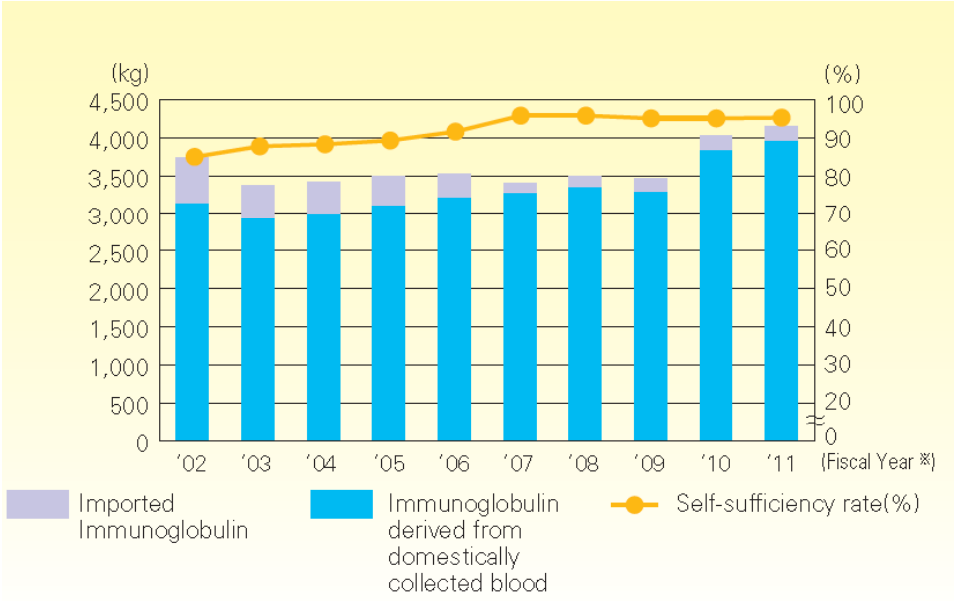
Plasma Products in Japan

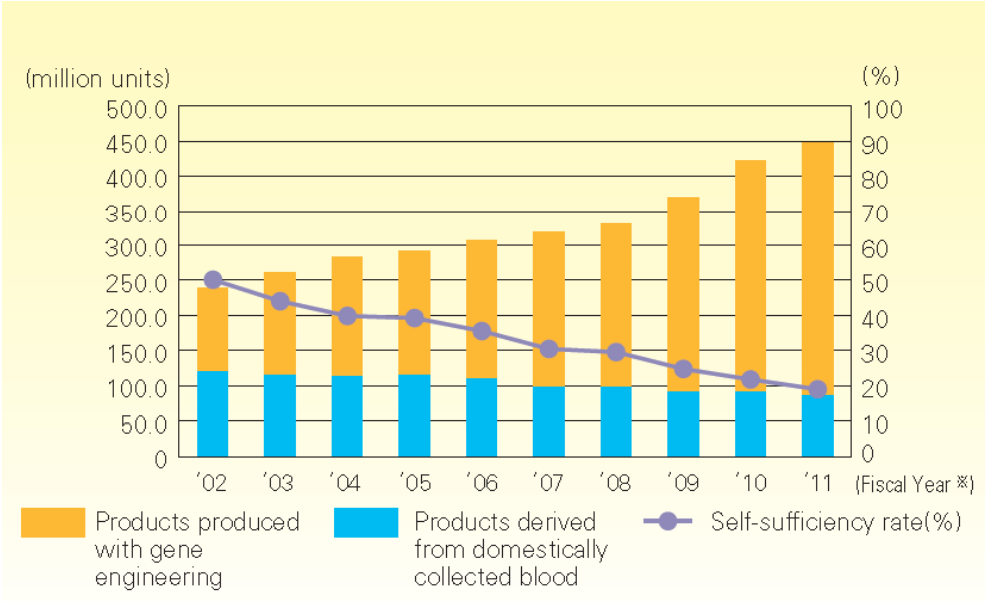
The grim consequence of self "sufficiency"

IGG



Usage ("self-sufficiency"100%) = 32.8 g/10^3

FVIII



Usage ("self-sufficiency"100%) = 3.6 IU/capita

Models of procurement

- For profit commercial sector through (mostly) source (apheresis) plasma from paid donors – predominantly from the USA

- Not for Profit sector through (mostly) plasma recovered from voluntary whole blood donors in the country of supply

- Contract manufacture of domestically procured plasma eg Australia, Italy, Spain

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Plasma collection by region

	2012		
	Recovered	Source	Total
Sub-total Asia & Oceania	921	3,568	4,489
Sub-total Latin America	359	34	393
Canada	157	-	157
United States	2,300	12,100	14,400
Sub-total North America	2,457	12,100	14,557
Sub-total Middle East/Africa	228	10	238
Sub-total Europe	3,926	1,616	5,542
Total World	7,890	17,328	25,218

How much plasma is needed? A proposed callibrator

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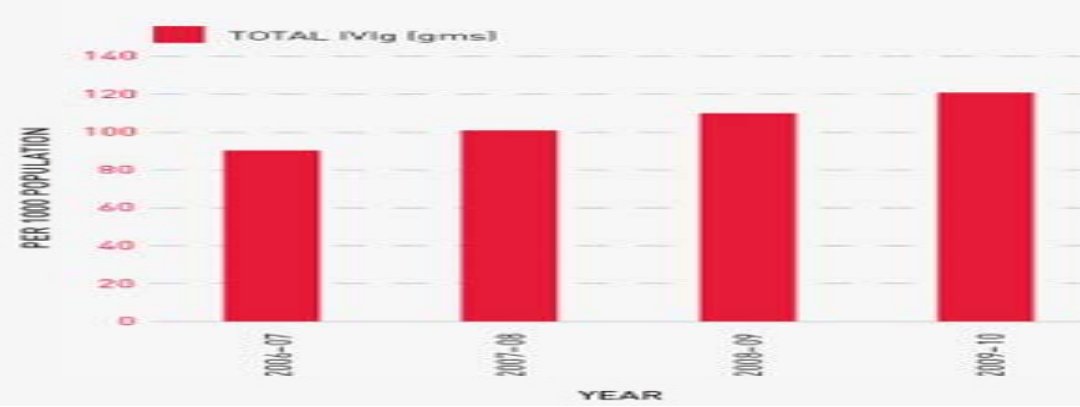
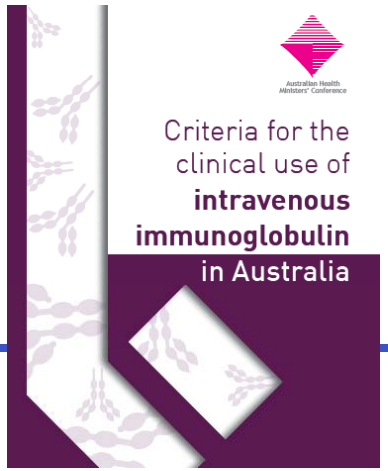
Australian Ig provision reflects many of WHO's policies

- Single government payer
- Product supplied free to all patients
- Expert advisory committee to reimbursement agency
- Evidence based guidelines
- Gate-keeping role – strict adherence to Level 1 indications



National Blood Aut
Australia



Australian Red Cross
BLOOD SERVICE

Plasma logistics

How Much?

- On the basis of
  - Usage of 120 g/10000 population
  - Ig yield of 4g/L of plasma

➢ **Ig needs can be met through 30L of plasma/1000 population**

➢ **This will also generate 6 IU/per capita FVIII**

From Where?

- Options for plasma procurement
  - Recovered from blood donations
  - Sourced from plasmapheresis
- If recovered
  - Assume 95% of donations are packed, each donation 250ml of plasma
    - ➢ ***Need to collect 126 units of whole blood per 1000 population !***

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Plasma Production

Country	Plasma production L/1000 population	Donor status
United Stated	66	Uncompensated and compensated
Austria	56.6	Uncompensated and compensated
Czech Republic	33	Uncompensated and compensated
Germany	31.6	Uncompensated and compensated
Australia	21.5	Uncompensated
Netherlands	18.8	Uncompensated
Denmark	17	Uncompensated
France	16.3	Uncompensated
Sweden	16.1	Uncompensated
Belgium	15.5	Uncompensated
(Japan)	7.6	Uncompensated

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Reflections

- The path of the rich countries is not necessarily the right one
- Many “rules” are not based on evidence and should be discarded, not imposed on economically restricted countries
- Evidence based plasma product demands exceed the supply
- Plasma procurement requires apheresis if supply is to be adequate and the blood system is to retain harmonious balance
- Impediments to access may well serve vested interests but harm patients

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And above all – remember this "rule"

I will apply dietetic measures for the benefit of the sick according to my ability and judgment; I will keep them from harm and injustice.