Plasma Protein Therapies

Cost – Effective and Evidence Based treatments

International Plasma Protein Congress

Dublin

March 5, 2013

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Pressures around access

- Perception that therapies are not ***cost-effective***
  - Tendency to ignore ***total medical costs***
- Perception that therapies are ***overused***
  - Myth of ***"off-label"*** use

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Health Technology Assessment
Role of Decision Analysis Modeling

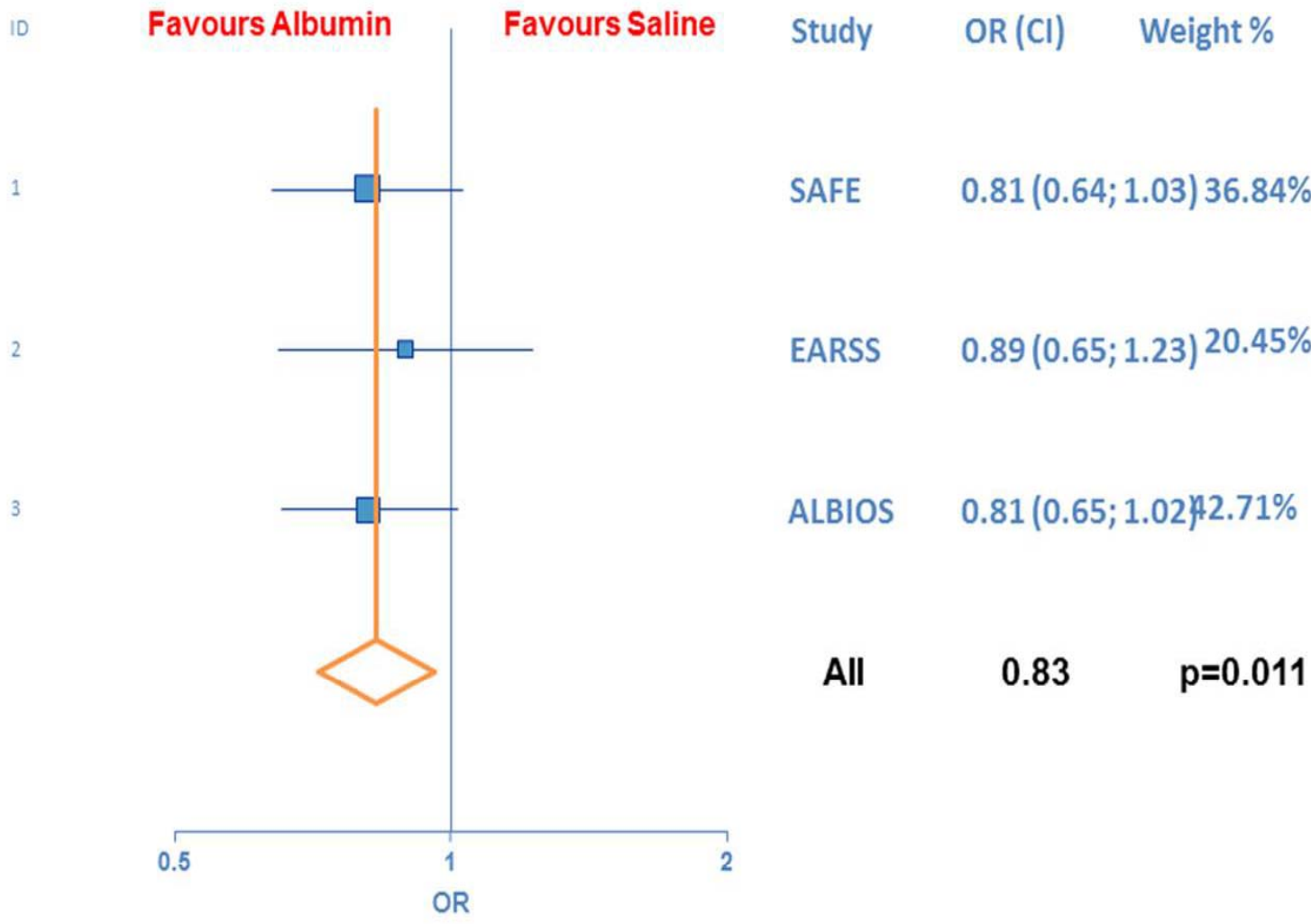
- HTA authorities and other policy/payer agencies increasingly use pharma-economic models to aid their decision making
- Models for PPTs have been developed and used
- In most instances, these have delivered negative outcomes for PPTs
- Important features of current therapeutic practice are being omitted from these exercises

Decision Analysis Model

- Clinical scenario – Patients in ICU with severe sepsis, treated with albumin or HES
- Hypothetical cohort – HCPU net population in US
- Presented
  - Sepsis 2011 Beijing 2011,the ISICEM Brussels 2012 & 2013, the ISBT Cancun 2012.
- Submitted for publication to Anasthesia & Analgesia 2013

Albumin in sepsis
Clinical studies – PPTA Meta-analysis

- Individual studies insufficiently powered to detect differences in mortality
- Meta-analysis by PPTA
- ***Significant benefit on survival from albumin***



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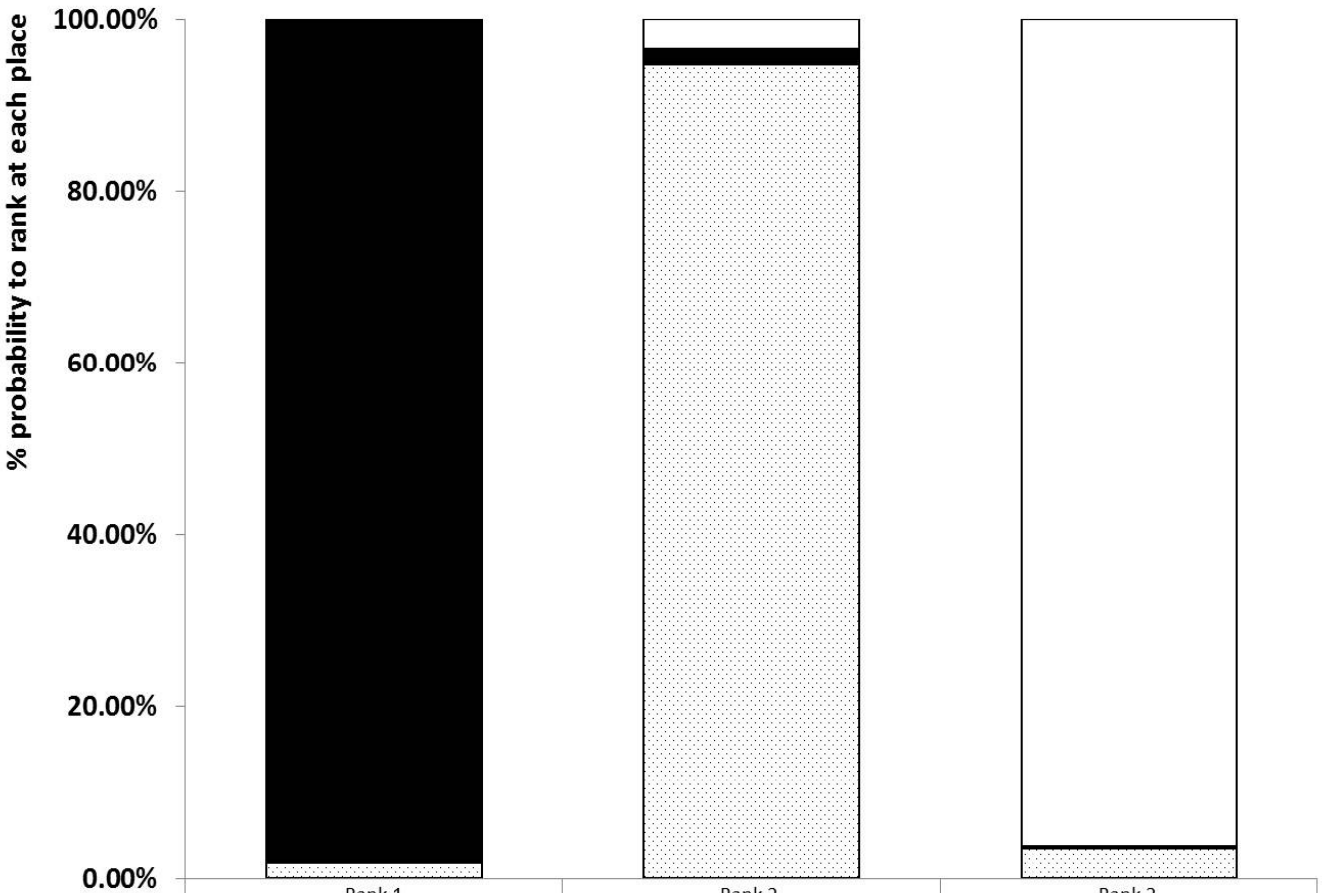
Decrease in mortality with colloids in sepsis Network meta-analysis (PPTA)



	Rank 1	Rank 2	Rank 3
HES	0.23%	3.48%	96.29%
Albumin	97.98%	1.76%	0.26%
Standard of Care	1.79%	94.76%	3.45%

Albumin deceases mortality

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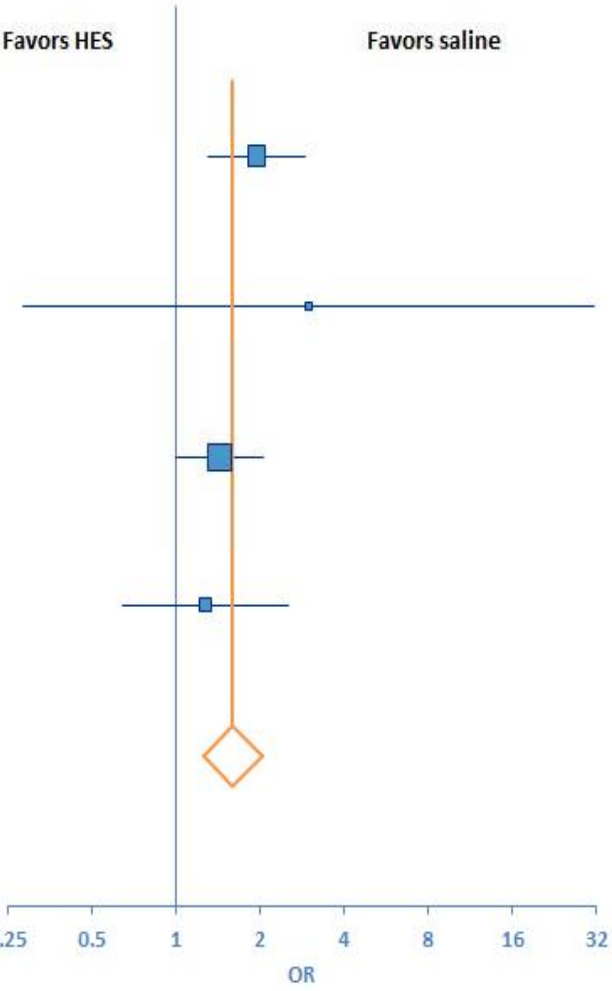
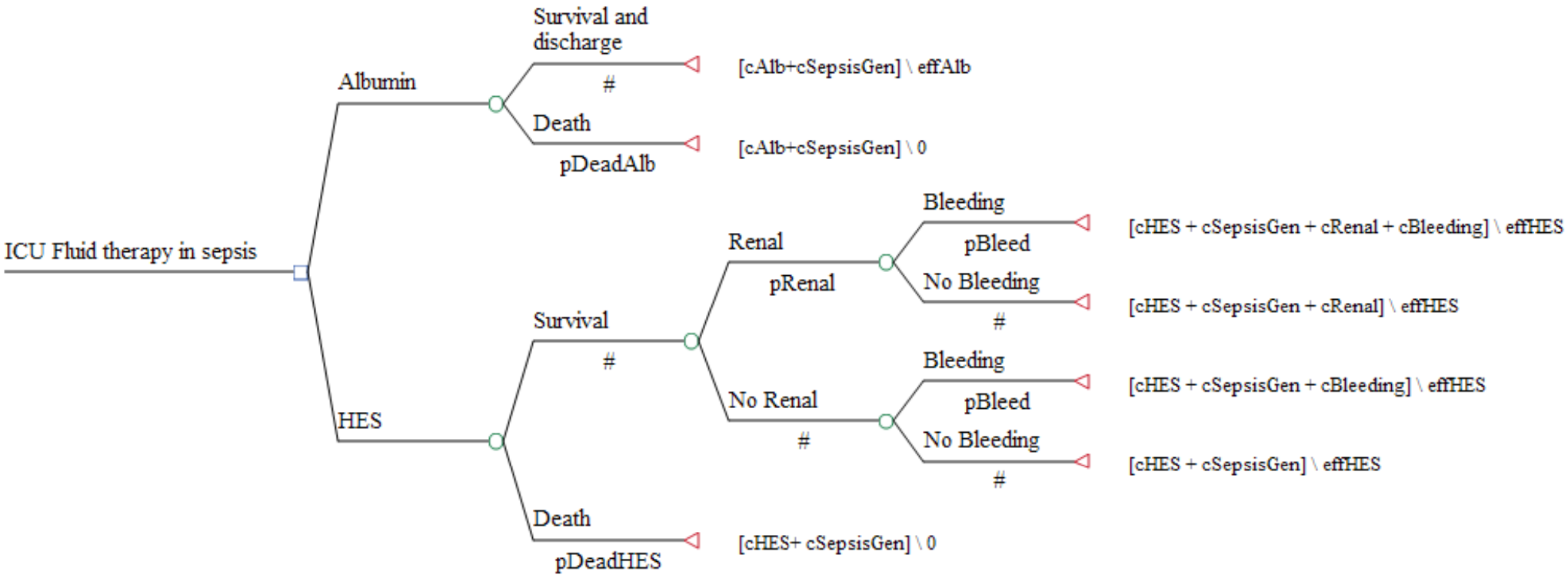
Renal Replacement Therapy in sepsis
Effect of fluid (Meta-analysis by PPTA)



Study	OR (95% CI)	Weight (%)
Brunkhorst (2008)	1.95 (1.3 - 2.9)	34.21%
Mcintyre (2012)	3.0 (0.28 - 31.6)	0.89%
6S (2012)	1.44 (1.01 - 2.06)	50.31%
CRYSTMAS (2012)	1.28 (0.65 - 2.53)	14.59%
Overall	1.61 (p-value: 0.0001)	

HES increases need for RRT

Basic structure of decision tree



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Results of Decision Model

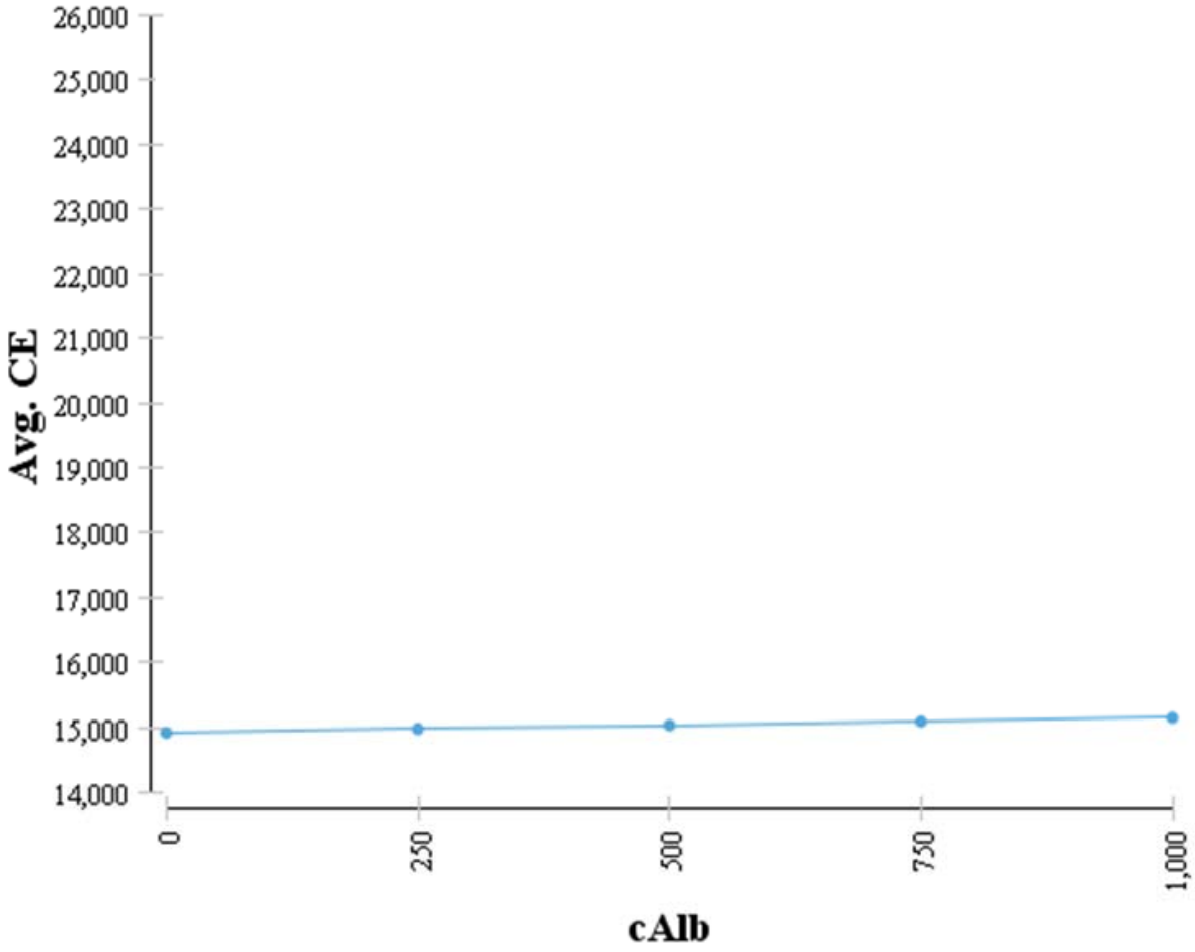
Strategy	Life Years Gained	Incremental Life Years	Total medical costs	Incremental Costs	ICER
HES	-0.69	-1.53	$48,488	$28,085	Dominant
Albumin	0.84		$20,403		

In sepsis

- **Albumin saves lives**
- **Albumin decreases costs**

Sensitivity analysis – cost of albumin

The price of albumin barely impacts on its cost-effectiveness in sepsis



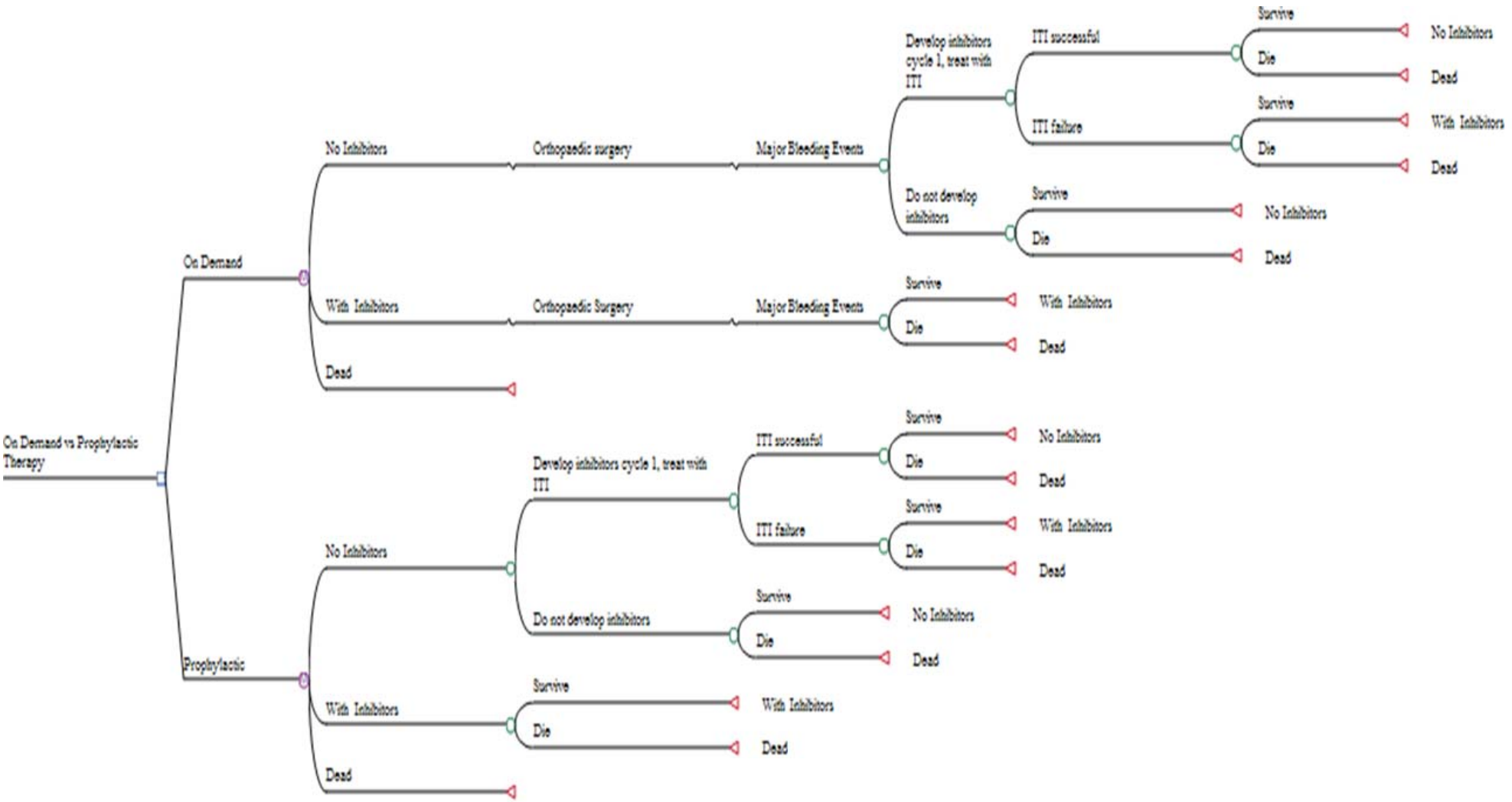
Cost Utility analyses (CUA) for PPTs

- CUA is the commonest form of health technology assessment
- Academic institutions advising reimbursement agencies
- Several CUAs have been published for PPTs
- Problematic features for rare, chronic disorders

New CUA for hemophilia treatment over whole of life

- As the hemophilia population ages, new evidence indicates that bleeding problems re-emerge
- It is important to continue treatment over the whole of life
- We have constructed a new CUA with previously unused features
  - Pharmacokinetic dosage
  - Effect on inhibitors
- Presented
  - WFH, Paris, July 2012, EU parliament Round table October 2012, EAHAD Warsaw February 2013
- In Press in Haemophilia 2013

Cost Utility analysis of prophylaxis vs OD therapy



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Prophylaxis in Haemophilia A Outcomes of Markov model

Payer Perspective	Cost	QALYs	Incremental Cost	Incremental QALYs	Cost/QALY	ICER
US						
OD	$4,140,275	19.42	$412,999	6.06	$213,759	$68,109
Pro	$4,563,274	25.48			$179,097	
UK						
OD	£1,784,095	27.16	- £280,866	9.69	£65,688	Dominant
Pro	£1,503,229	36.85			£40,798	
Sweden						
OD	SEK 22,101,124	17.87	SEK 5,331,051	10.99	SEK 1,236,772	SEK 484,888
Pro	SEK 27,432,176	28.87			SEK 950,197	
Sweden (Daily Pro dosing)						
OD	SEK 22,101,124	17.87	- SEK 10,541,993	10.99	SEK 1,236,772	Dominant
Pro	SEK 11,559,131	28.87			SEK 400,386	

In all three perspectives, prophylaxis shows cost effectiveness to a level accepted by each country's payers

Model Results – Cost Effectiveness relative to Willingness to Pay

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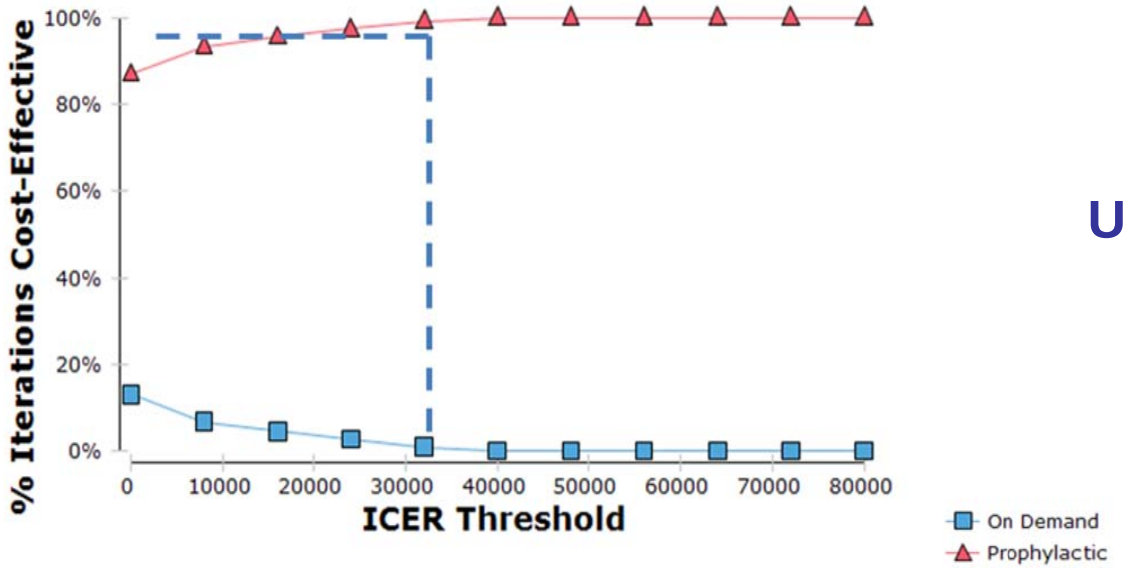
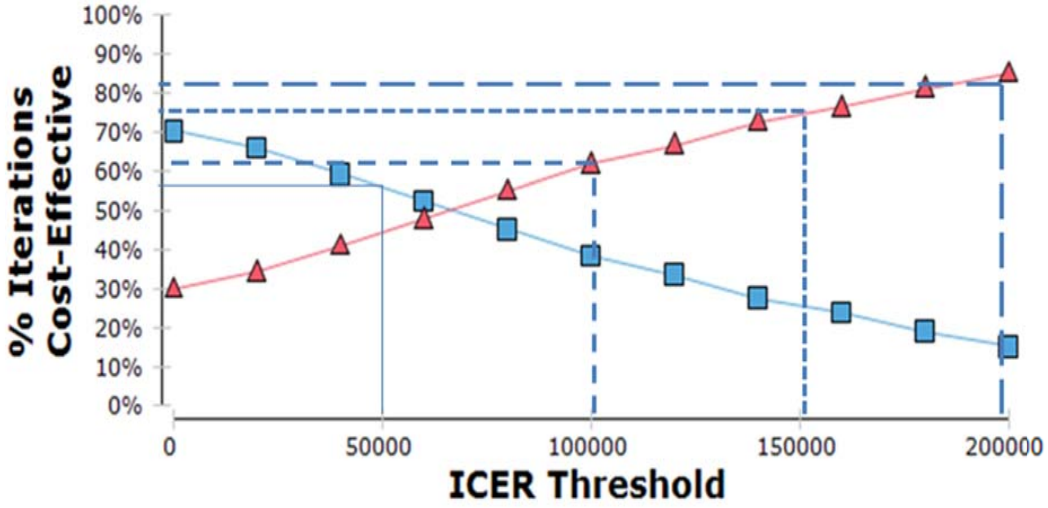


UK



USA

- **Prophylaxis is always cost-effective in the majority of assessments**

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Are plasma protein therapies over-used?

- Wide variation between countries
  - Dosage
  - Prevalence
- Controversies regarding indications
  - “off-label”
  - Guidelines
  - EBM-Cochrane
- Level of care
  - Prophylaxis

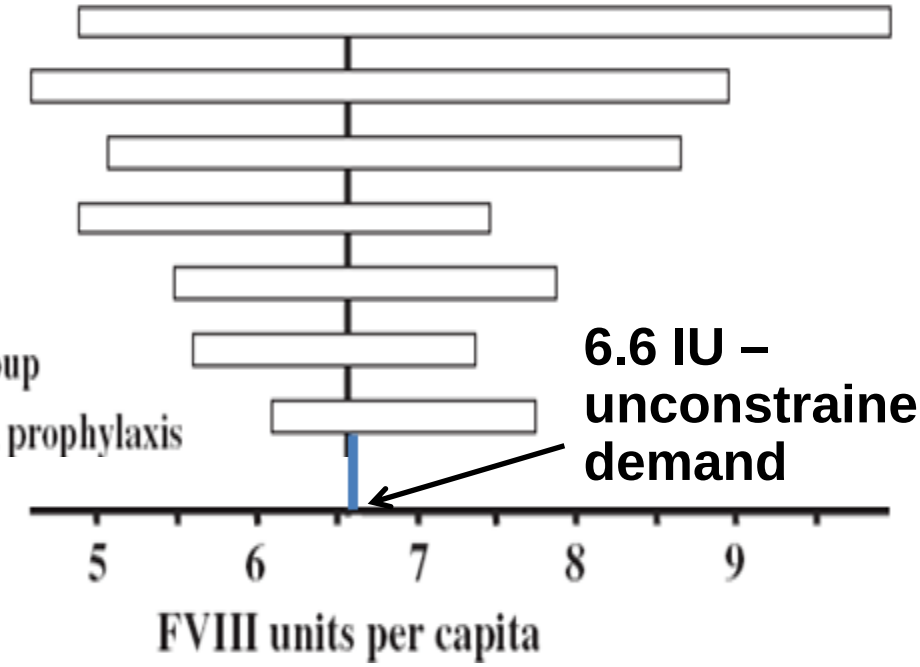
The concept of Latent Therapeutic Demand Stonebraker 2004 et seq

Latent therapeutic demand **(LTD) is the underlying demand that represents how physicians would prescribe treatment and how patients would follow or comply with the prescribed treatment if ample supplies of drugs were available and affordable**

LTD in haemophilia
Factors impacting on FVIII demand

*Prophylactic dosing
*Prevalence
*Severity
*Number of prophylactic infusions administered
*Weight in the ≥ 21 age group
*Prophylactic treatment rate for severe haemophilia A in the ≥21 age group
*Number of bleeding episodes for severe and moderate haemophilia A on prophylaxis

*Variables with the greate stimpact on unconstrained FVIII demand



Haemophilia (2004), 10, 18–26

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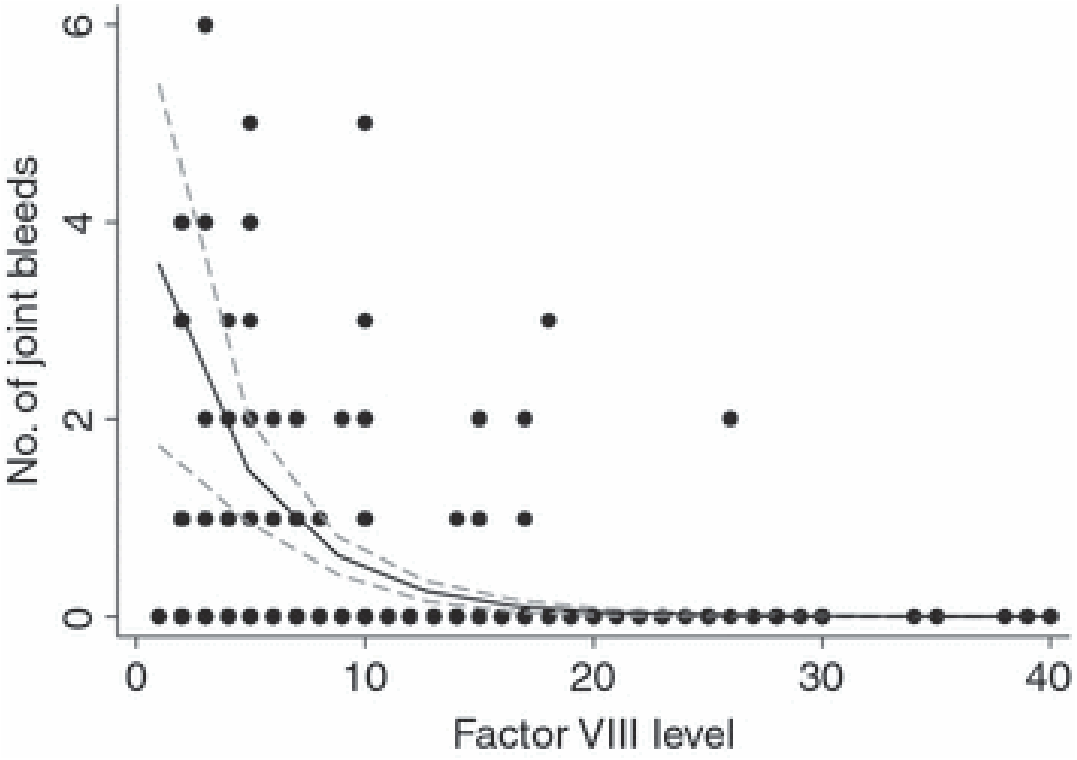
How much FVIII? Bleeds vs factor levels



Haemophilia Volume 17, Issue 1, pages 41-44, 2 SEP 2010

- **Full protection from bleeding only occurs at 15% FVIII**
- **BUT – current prophylaxis regimens aim for 1-2% trough levels**
- **As treatment continues to improve – WE MUST ANTICIPATE MORE DEMAND FOR FVIII**

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LTD for IG

(1) Focus on CVID and XLA.

(2) Identified and defined the variables impacting LTD for PID through literature review , data base interrogation (ESID) and discussions with experts (J Orange, I Quinti).

(3) Obtained range estimates for each variable from published articles.

(4) Conducted sensitivity analysis to order variables in terms of their impact on LTD for PID.

(5) Modeled the uncertainty surrounding the most sensitive variables.

(6) Presented at the Clinical Immunology Society Third Annual Meeting, Chicago May 2012, submitted to the ESID Congress, Florence, October 2012, scheduled for ESID Congress, Florence Oct 2012

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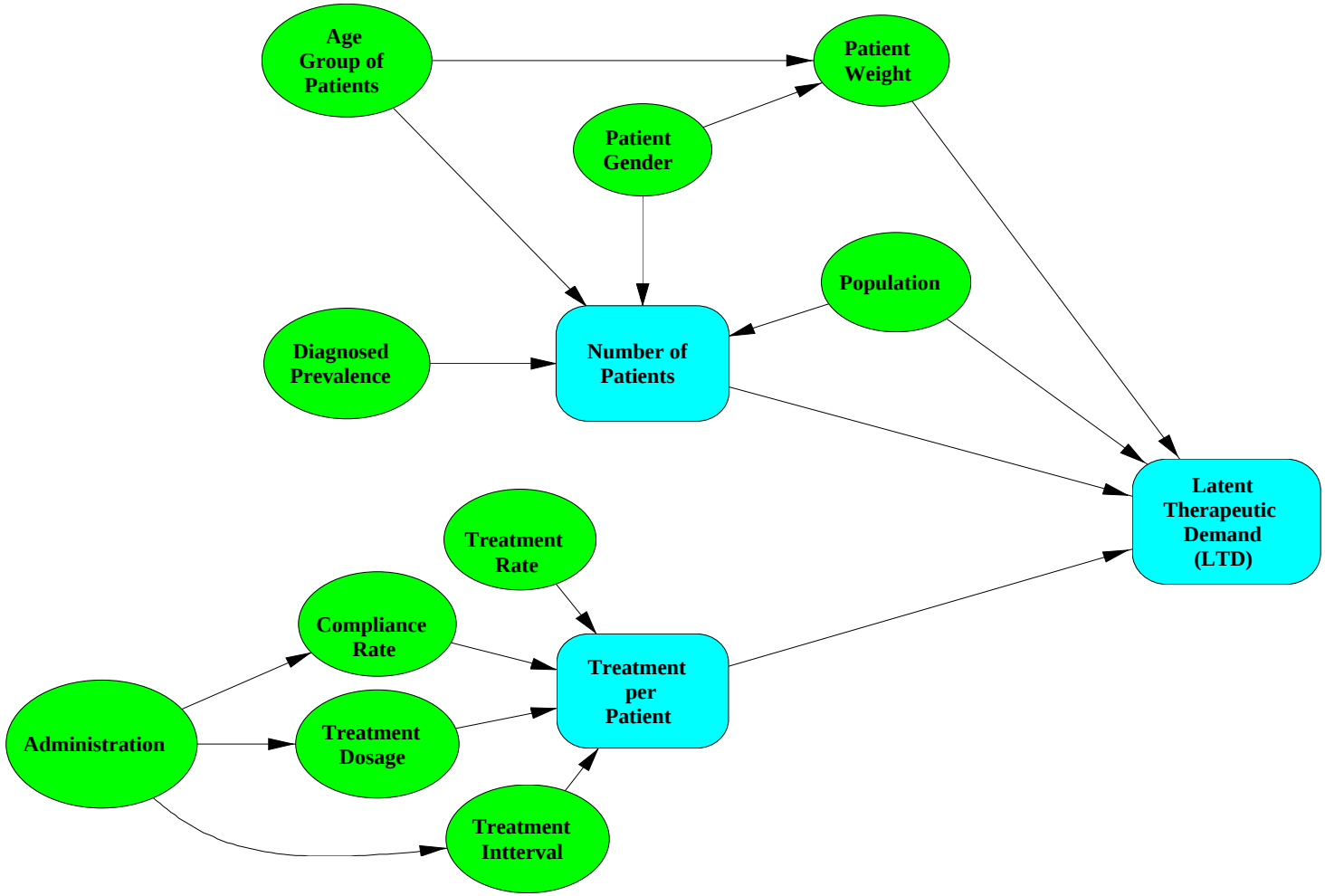
Integration of variables into model

Epidemiology Related Variables

Treatment Related Variables



Results

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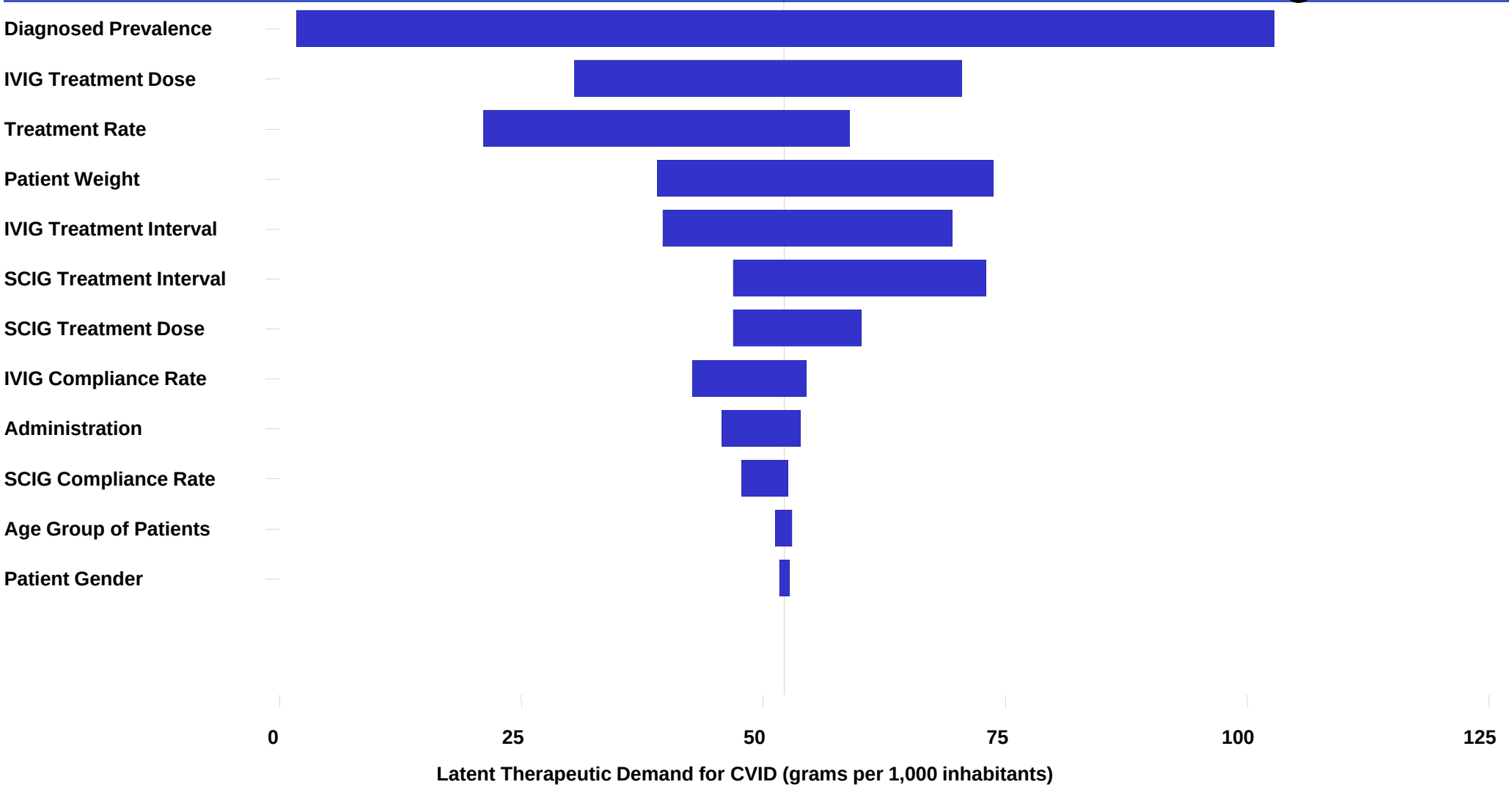
Diagnosed prevalence is the key driver for LTD of Ig in CVID



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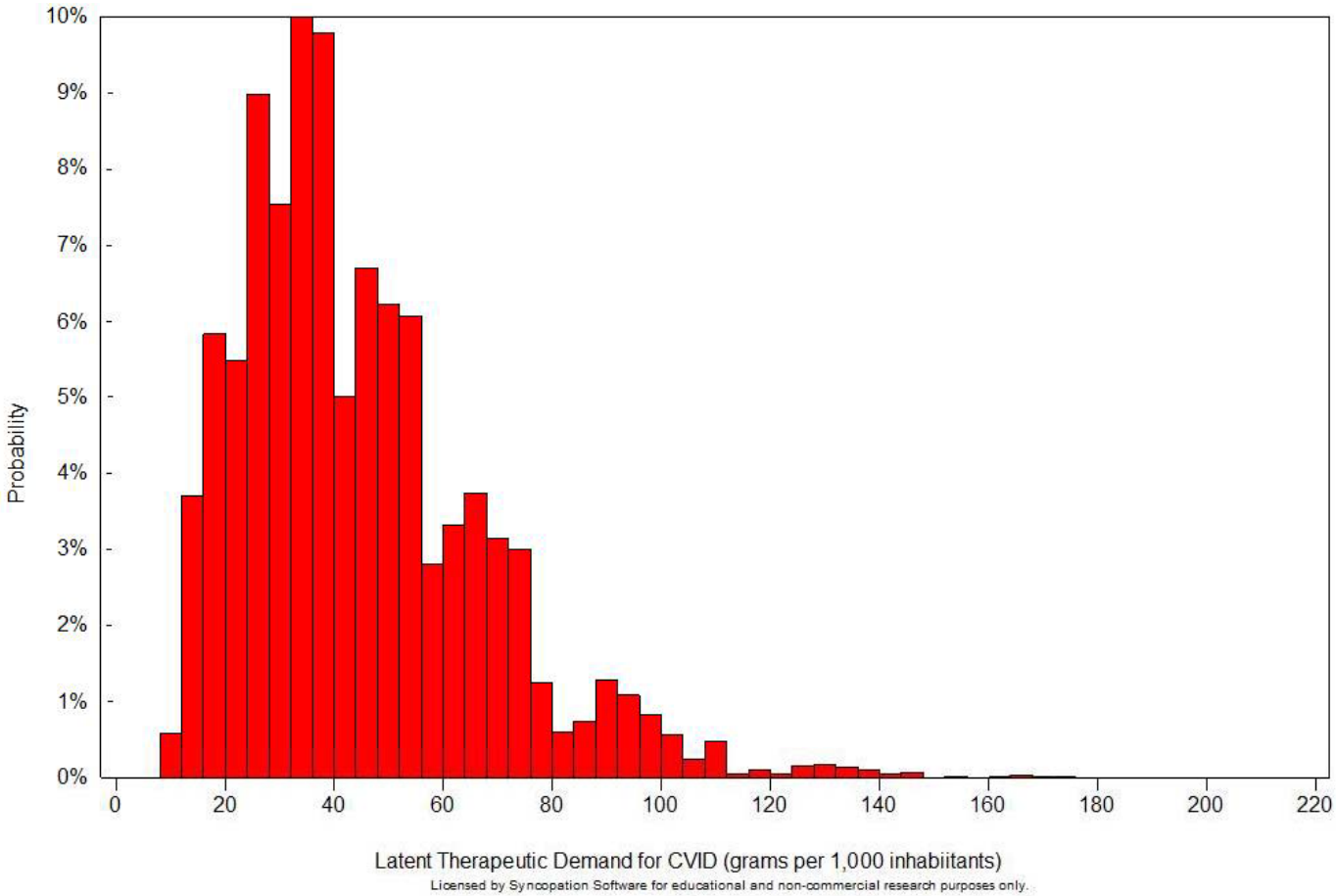
CVID

- *The IG latent therapeutic demand (LTD) for the treatment of CVID alone is larger than most countries' IG consumption across all disease indications.*
- *Using this model, the LTD for CVID + XLA ≅100 g/1000 population.*



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Evidence level of IG indications

American Academy of Allergy, Asthma and Immunology

Disease	Benefit	Evidence level	Strength of recommendation
PID	Definitely beneficial	IIb	B
Chronic lymphocytic leukemia with reduced IgG and history of infections	Probably beneficial	Ib	A
ITP	Definitely beneficial	Ia	A
GBS	Definitely beneficial	Ia	A
MMN	Definitely beneficial	Ia	A
CIDP	Definitely beneficial	Ia	A

Orange et al J ALLERGY CLIN IMMUNOL APRIL 2006

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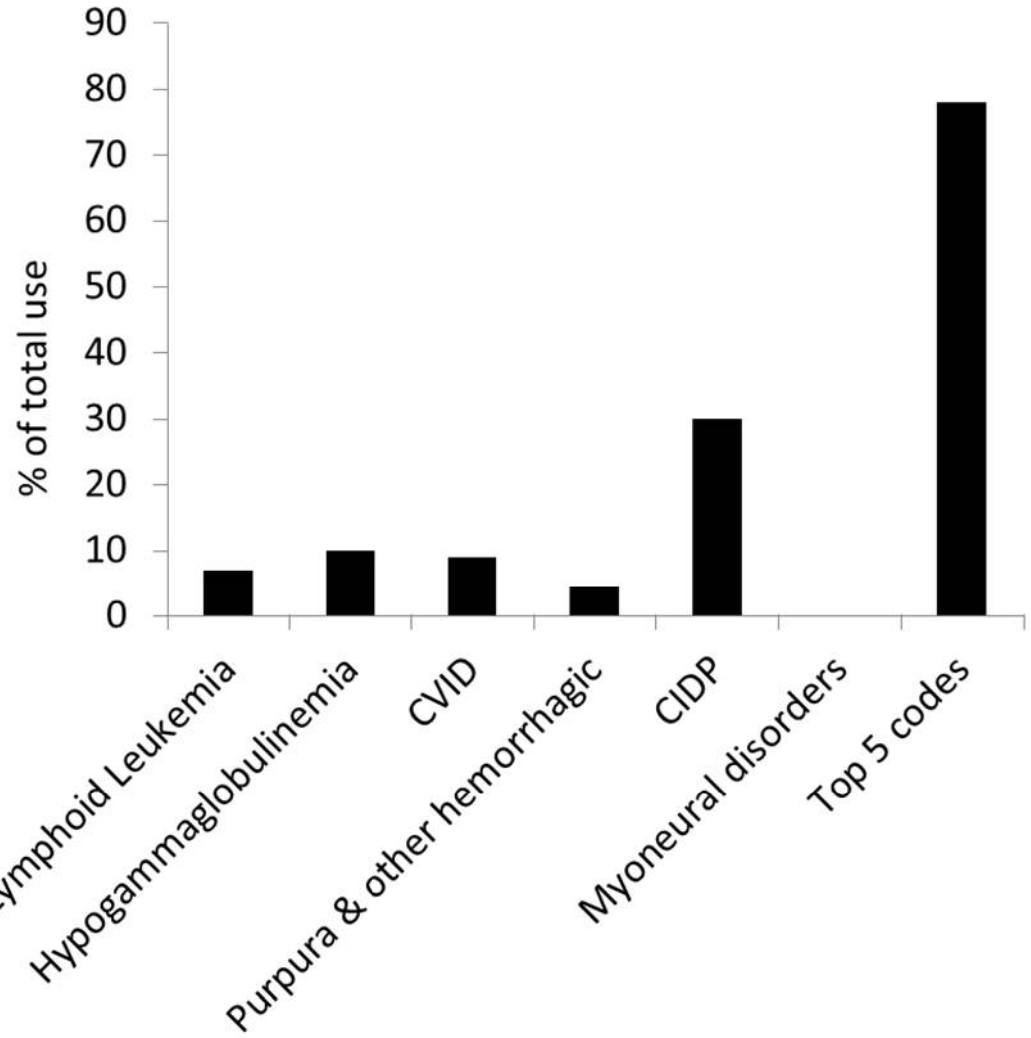
IG use in USA Physicians' Offices

All high evidence indications



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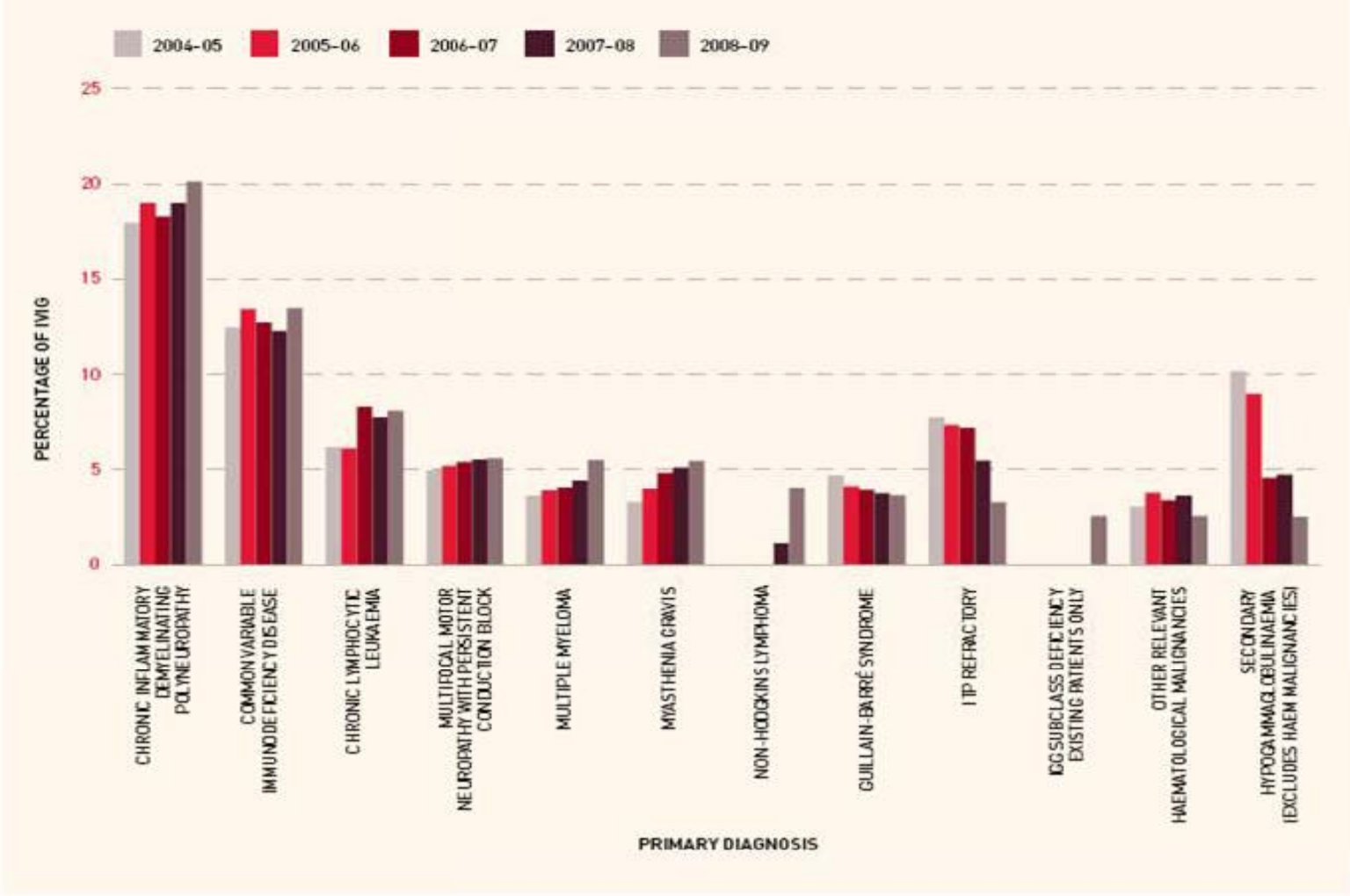
IG Use in Australia

All high evidence indications



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Conclusions

We can show, though hard data and methodology accepted by the peer review environment, that the main plasma protein therapies:

- ***Are cost-effective***
- ***Are used on the basis of the best clinical evidence***
- ***Are needed in larger amounts than now supplied by the relevant patient communities***