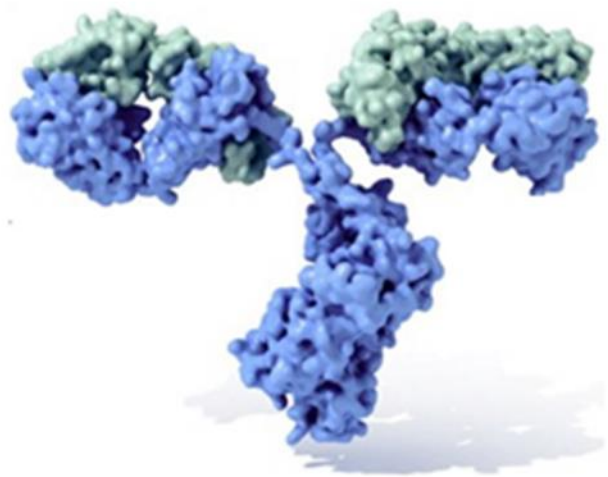
SAFETY AND EFFICACY OF IMMUNOGLOBULIN THERAPIES FOR PRIMARY IMMUNODEFICIENCIES



A GUIDE FOR USERS, ASSESSORS AND FUNDERS

ALBERT FARRUGIA

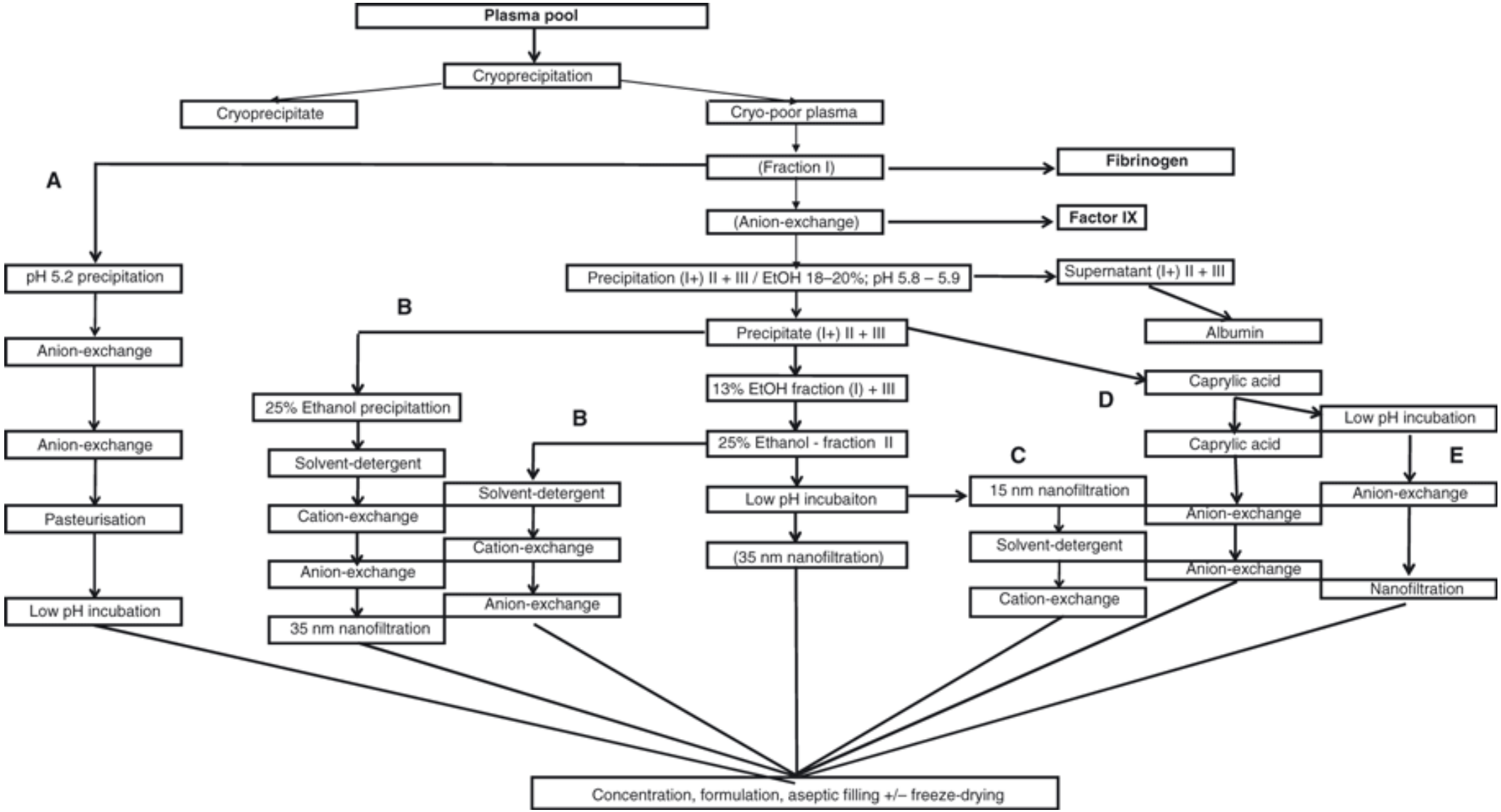
2011 - 2018

A Guide for users, assessors and funders

IPOPI
INTERNATIONAL
PATIENT ORGANISATION
FOR PRIMARY IMMUNODEFICIENCIES

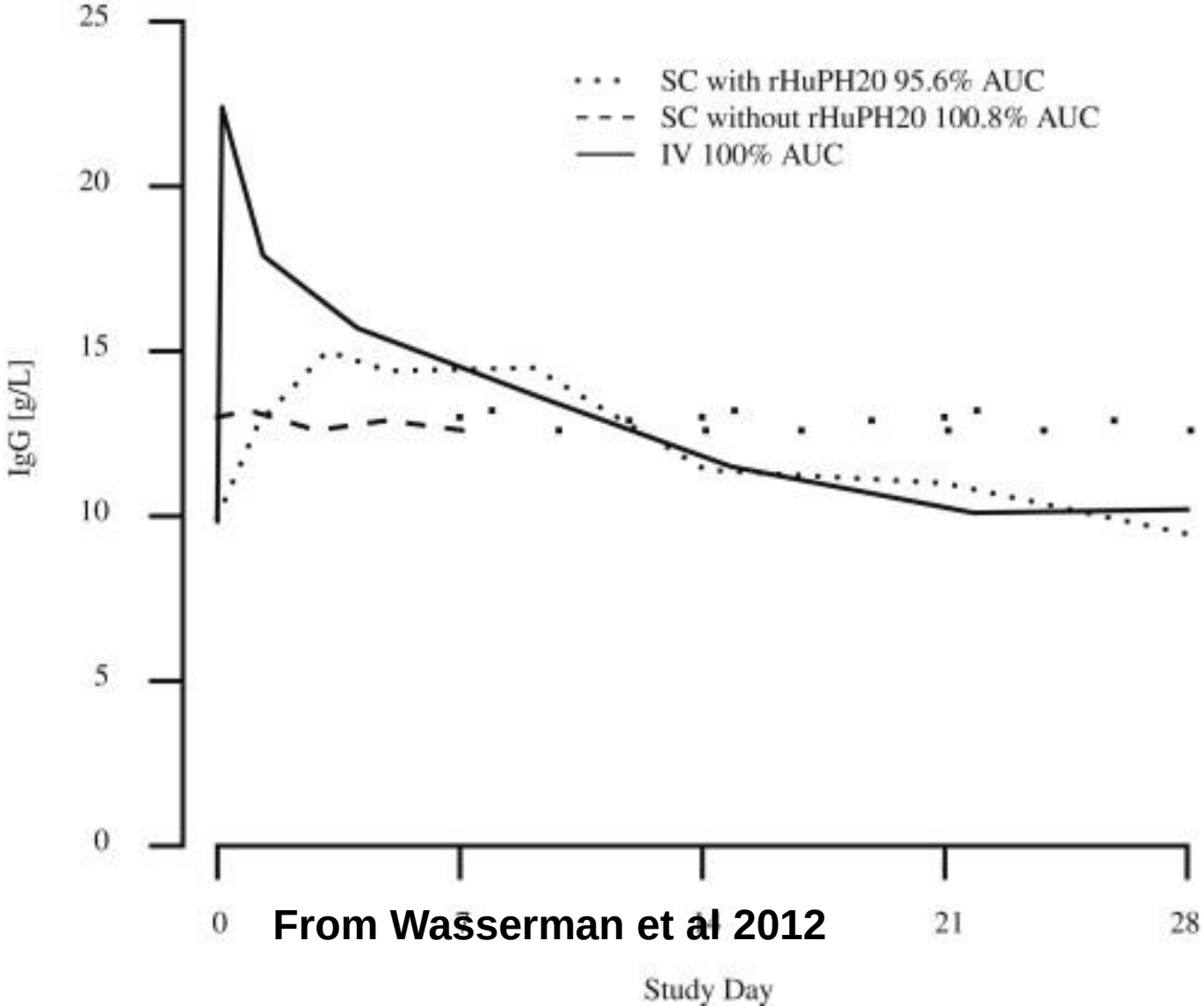
Prepared for IPOPI by Prof Albert Farrugia

Intravenous immunoglobulin G: trends in production methods, quality control and quality assurance



Vox Sang, Volume: 98, Issue: 1, Pages: 12-28, First published: 09 December 2009, DOI: (10.1111/j.1423-0410.2009.01226.x)

Serum IgG concentration following infusion of IVIG, SCIG and SCIG with recombinant hyaluronidase to facilitate access.



From Wasserman et al 2012

Personalising treatment – do no harm

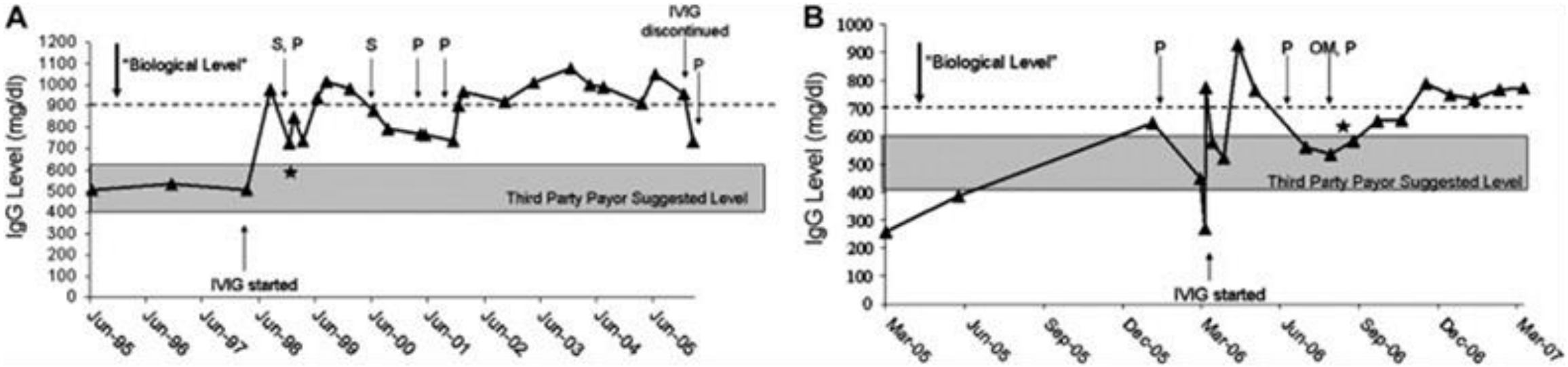


Figure 3 IgG trough levels in two individual PID patients A and B before, during, and after initiating IVIG therapy and associated infection history. ∗Time at which patient was put in practice which dosed on basis of biological, rather than guideline driven, through level. S, Acute sinusitis; P, pneumonia; OM, otitis media. J Allergy Clin Immunol. 2008 Jul;122 (1):210-2

Personalising treatment – tailor treatment

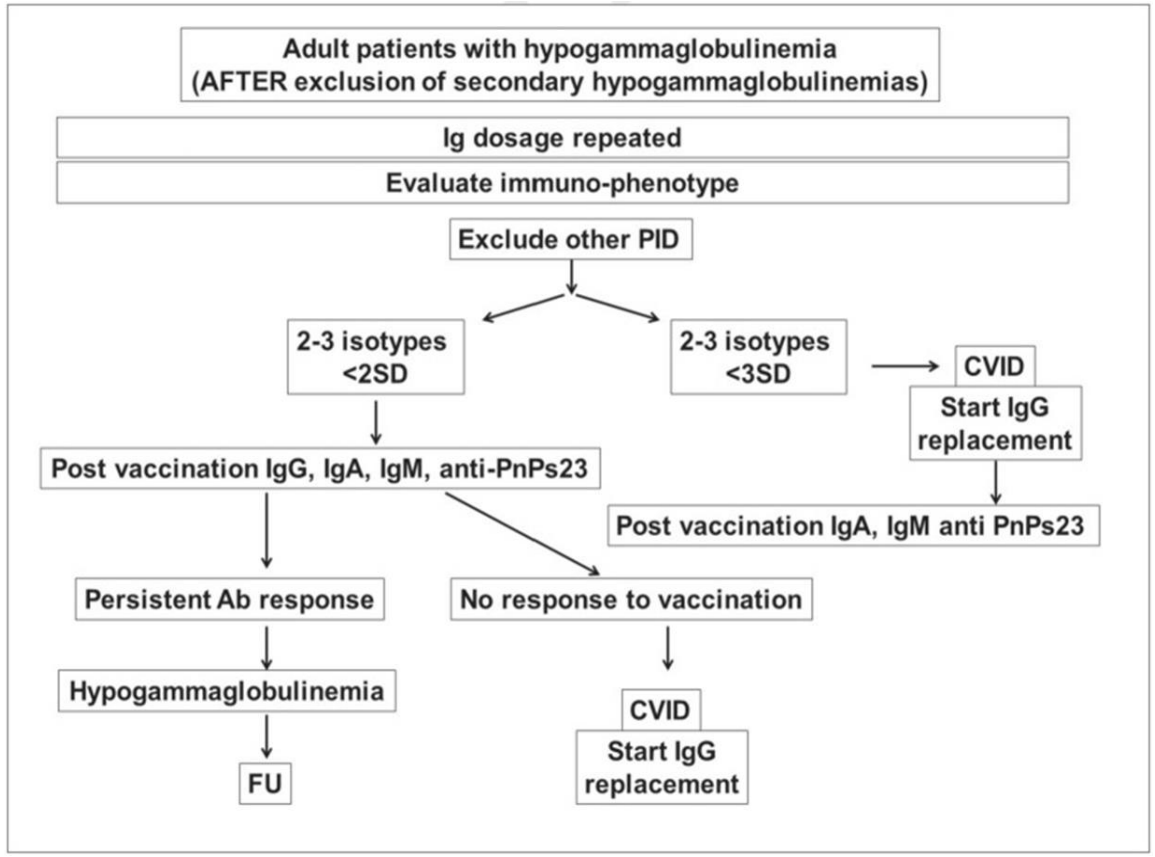
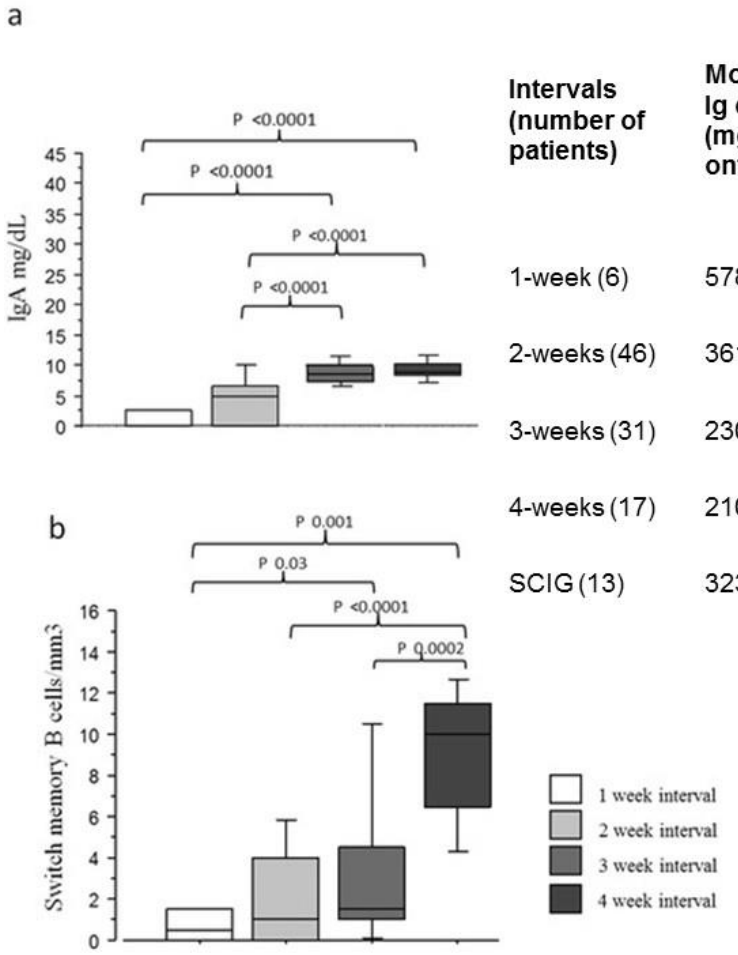


Figure 4 Algorithm for diagnosis in patients with hypogammaglobulinemias. Legend Ig: immunoglobulins; PID: Primary Immune Deficiencies; Ab: antibodies; PnPs23: 23-valent pneumococcal polysaccharides; FU: follow up; SD: standard deviation. Blood Transfus 2013; 11 Suppl 4: s40-4

Personalising treatment – dosages can be adjusted



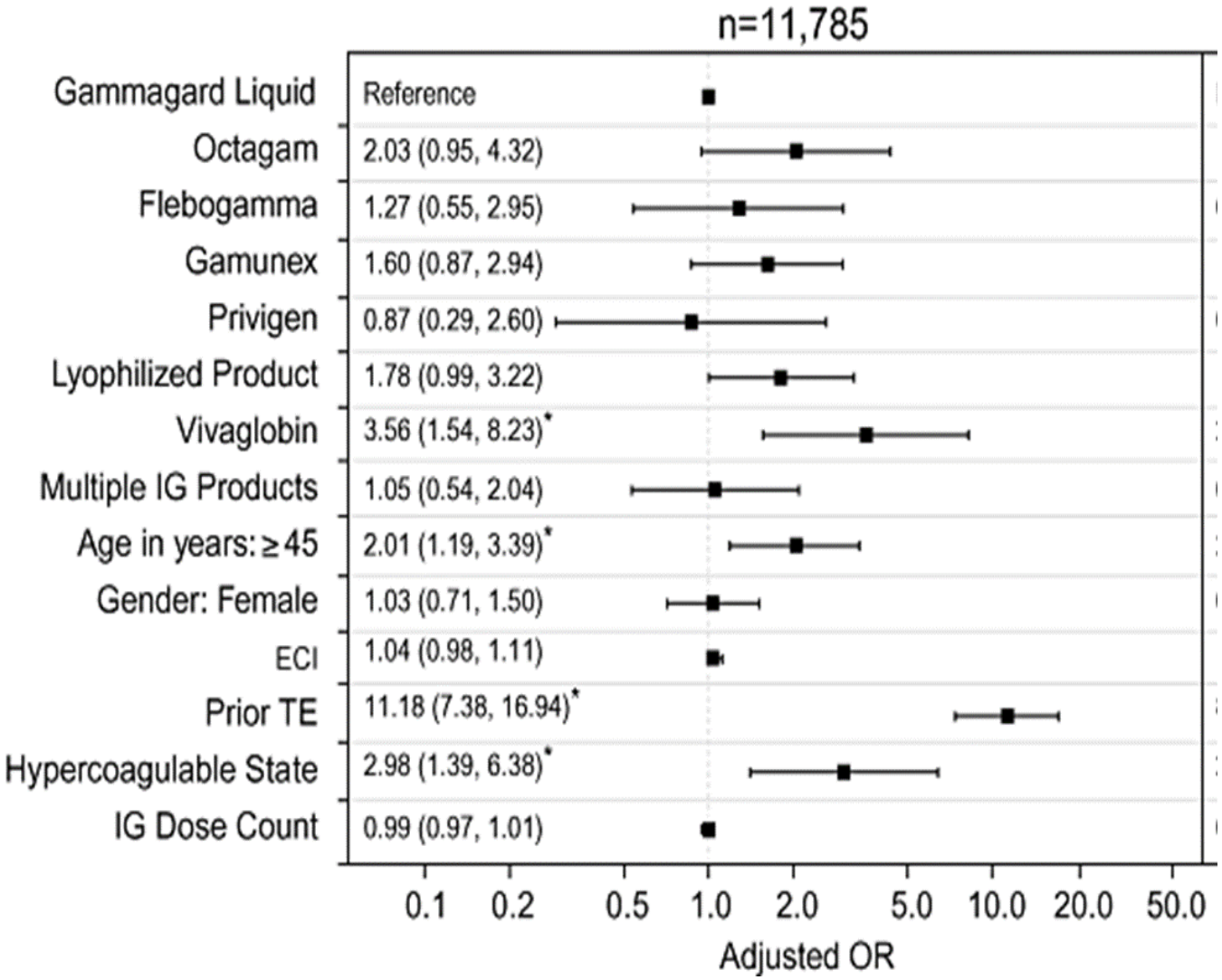
Intervals (number of patients)	Monthly Ig dose (mg/kg/month)	IgG trough levels (mg/dL)	IgA levels (mg/dL)	Switched memory B cells (%)
1-week (6)	578 ± 70	595 ± 88	1 ± 2.5	0.7 ± 1
2-weeks (46)	361 ± 103	693 ± 131	4 ± 4	2.6 ± 3.7
3-weeks (31)	230 ± 71	657 ± 103	9 ± 1	3.5 ± 3.0
4-weeks (17)	210 ± 93	615 ± 84	9.5 ± 2	8 ± 4.6
SCIG (13)	323 ± 91	641 ± 164	20 ± 19	7.5 ± 4.9

Figure 5 Dosage regimens for PID patients grouped according to clinical/laboratory phenotypes. From J Clin Immunol. 2014; 34(7): 813–819

Adverse events as a result of IgG therapy

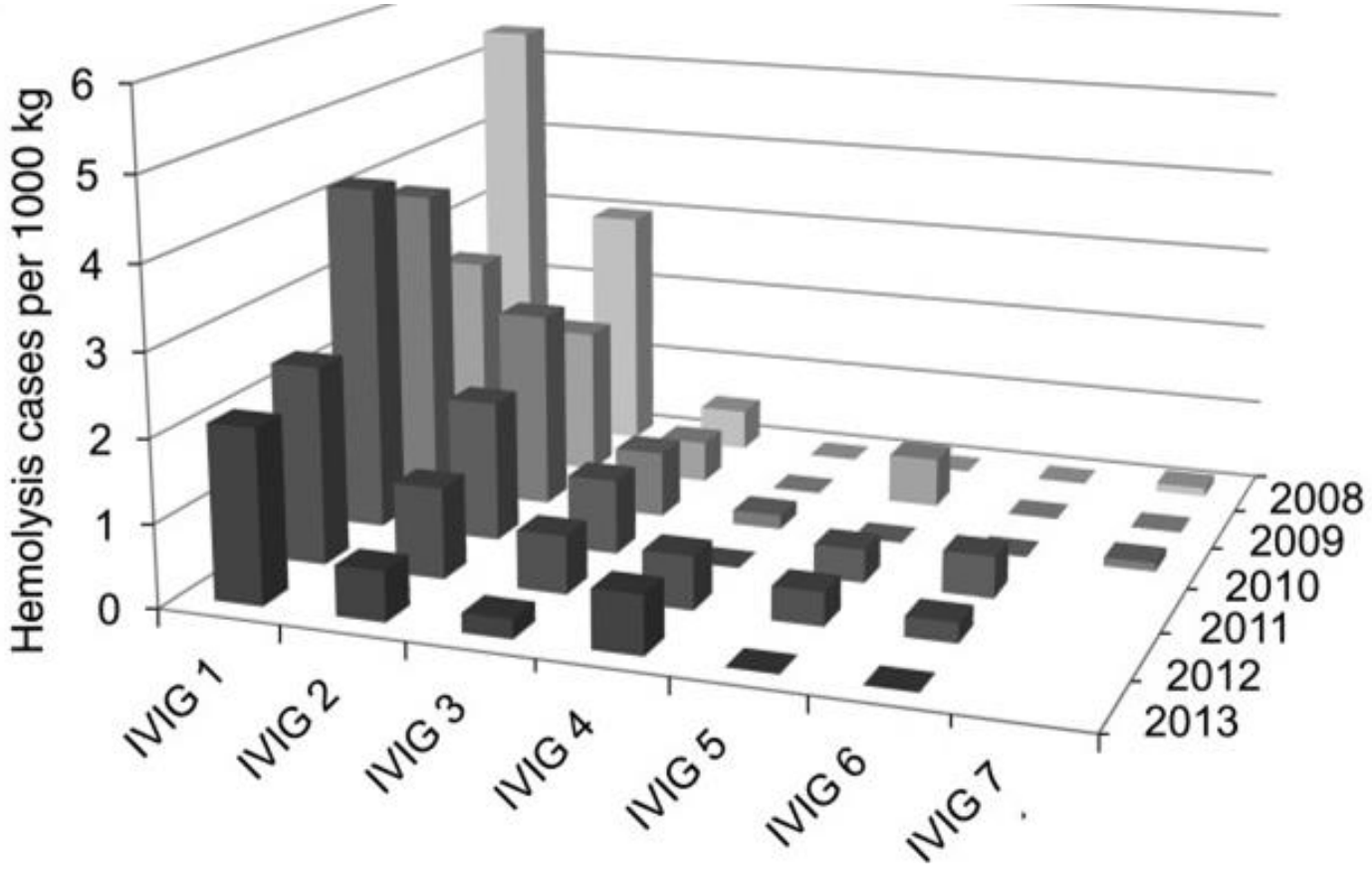
Adverse Event	Examples
Infusion Reactions	Non-anaphylactic: headache, chills, low-grade fever, flushing, back or abdominal pain, nausea, myalgias, hypotension. Associated with release of TNF and/or PAF. Anaphylactic: flushing, swelling, dyspnea, hypotension, nausea, vomiting, vascular collapse and rarely death. Associated with IgA deficiency and either IgG or IgE antibodies against IgA
Vascular Events	Congestive heart failure Thromboembolic events
Renal failure: oliguric renal failure wi th high sucrose preparations. On biopsy renal tubular epithelial cells are swollen and contain va cuoles Aseptic meningitis	
Hematologic events	Hemolytic anemia Neutropenia
Pulmonary edema and transfusion-related acute lung injury	
Infections	Hepatitis C Parvovirus B19
Skin rash	
PAF = Platelet activating factor TNF = Tumor necrosis factor	

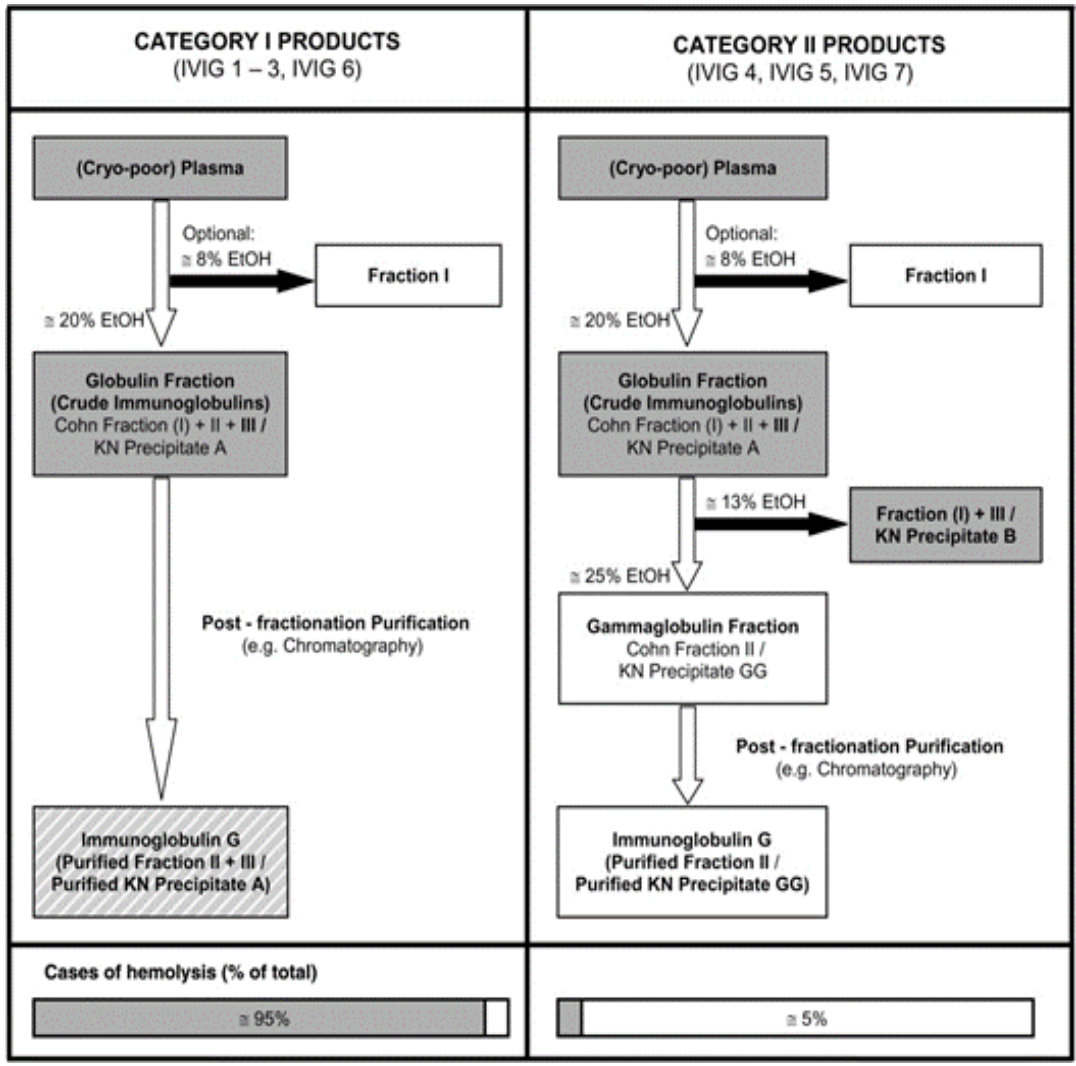
Association between different immunoglobulin products and risk of thrombotic events

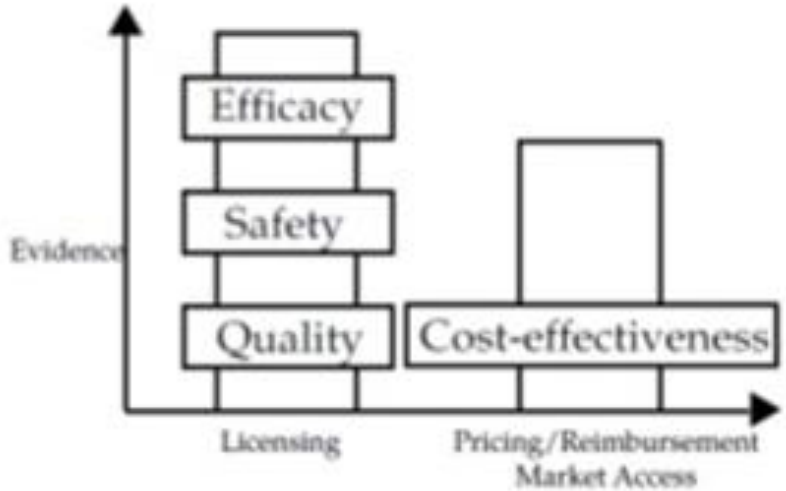


Sensitivity analyses of the association between different immunoglobulin products and risk of thrombotic events. From Daniel et al 2012

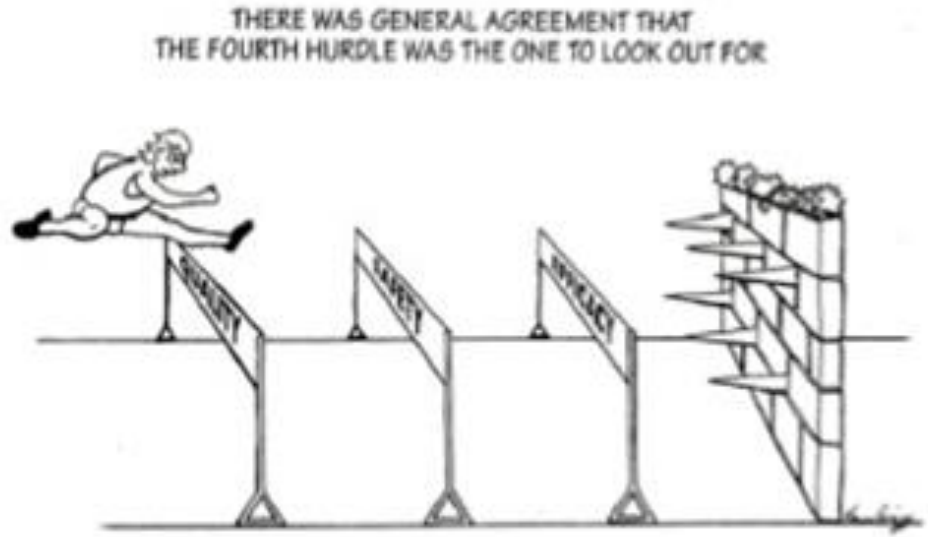
Haemolysis following IG products



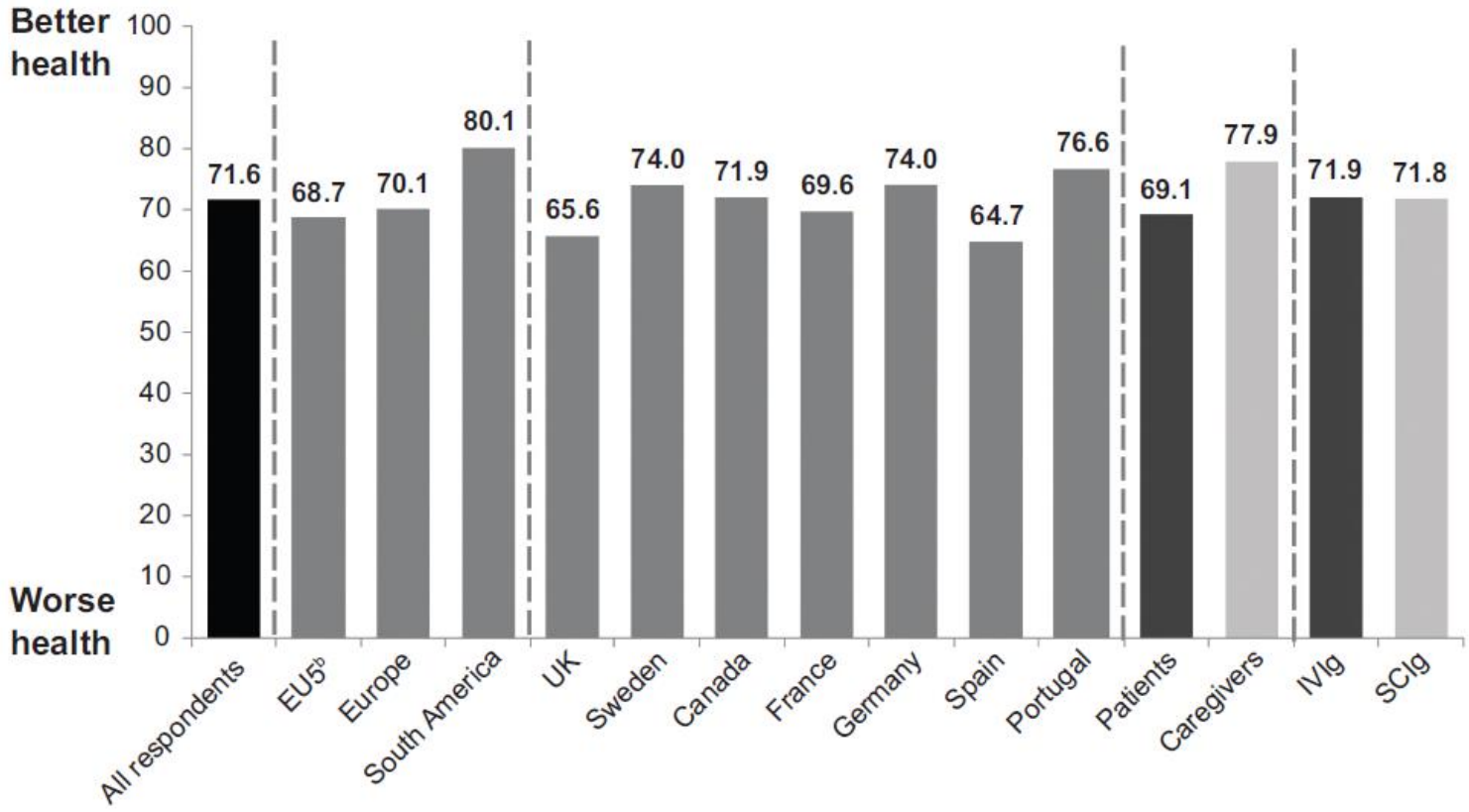




Cost-effectiveness (or CER) has became the "fourth hurdle" to market access

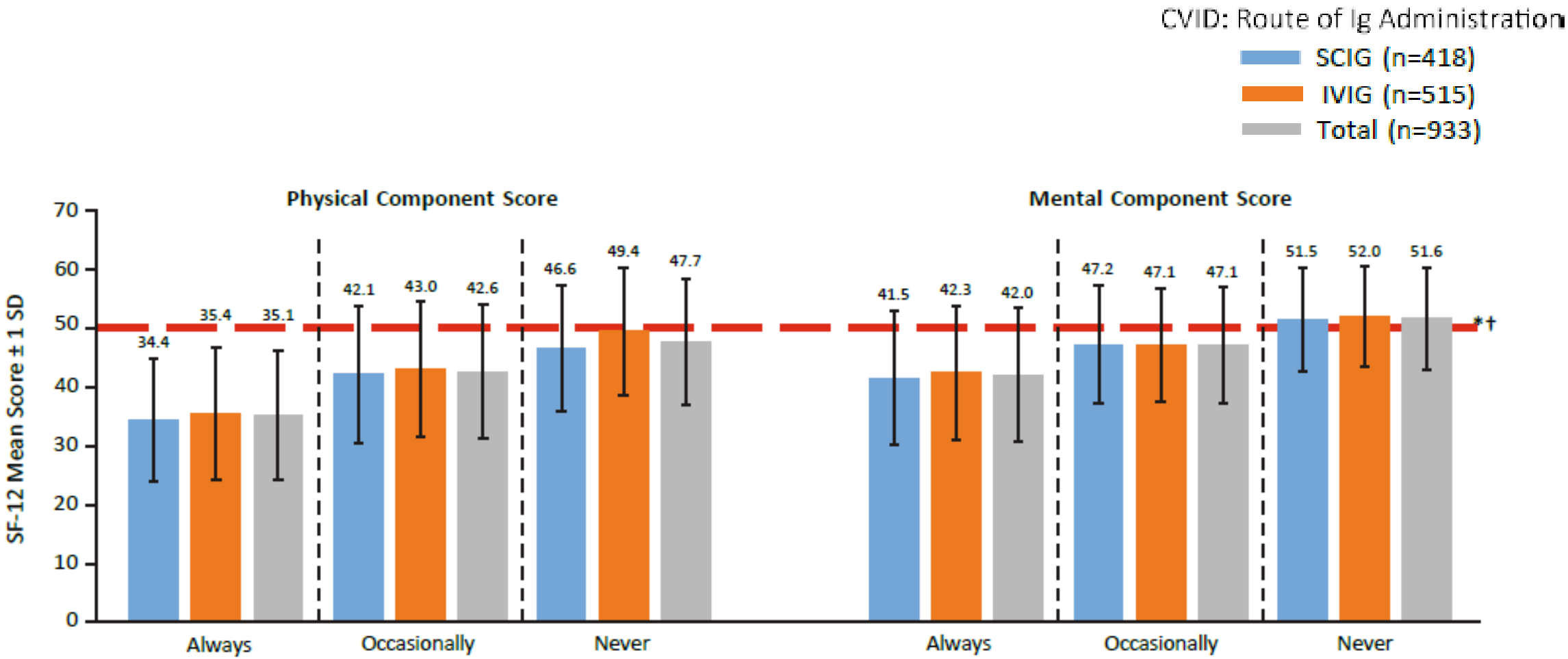


Health of patients with primary immunodeficiency disease
Country and route of immunoglobulin administration
IPOPI Survey



Patient Preference and Adherence 2014:8 621–629

No significant difference in HRQOL between IVIG and SCIG IDF Survey



J Clin Immunol (2017) 37:461–475

Choosing and paying for Ig products for PID

- Ig products have increased and enhanced the lives of patients with PID
- The number of these products has increased in number in concentration, mode of and speed of administration, and all are safe and effective
- Adverse events studied over the past decade show that caution is necessary when modifying technology for reasons of commercial advantage or patient convenience
- Guideline-driven dosage protocols are now under pressure in the era of personalised medicine
- Health technology assessments need to be based on real data involving patient preference