



IPOPI 4TH REGIONAL ASIAN PID MEETING

19-20 NOVEMBER 2022
KUALA LUMPUR, MALAYSIA

an IPOPI event

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Ivlg & SCIg – life style considerations

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IPOPI doctors-patients meeting, Kuala Lumpur, November 19th, 2022

speaker

Disclosure

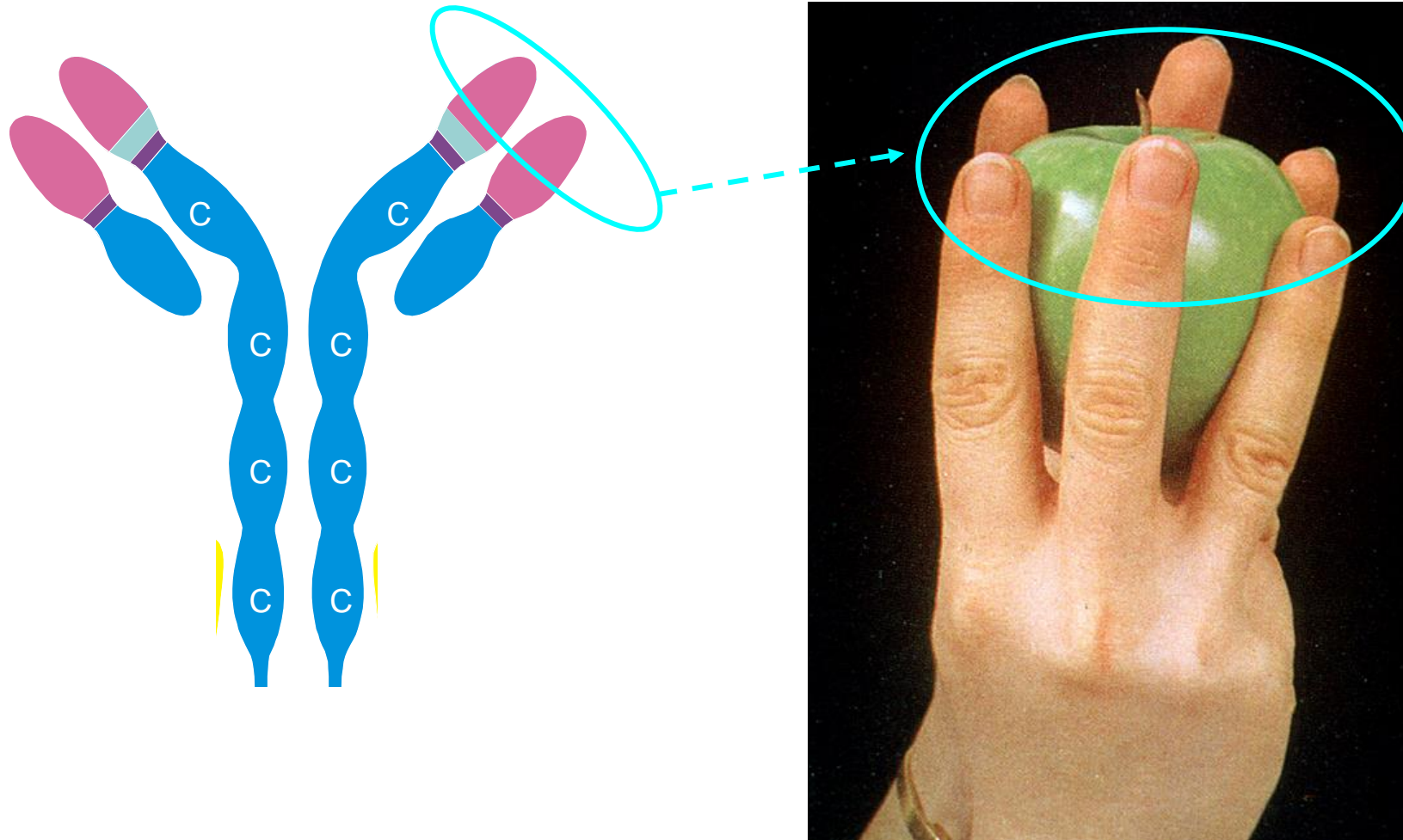
	Companies/organisations
<ul style="list-style-type: none">• Sponsors research• Travel support• Stock• others...	<ul style="list-style-type: none">• JMF, CSL Behring, Novartis, NWO

IvIg & SCIg – life style considerations

- Immunoglobulin therapy
- Personalizing IgG therapy
- The future
- Conclusions

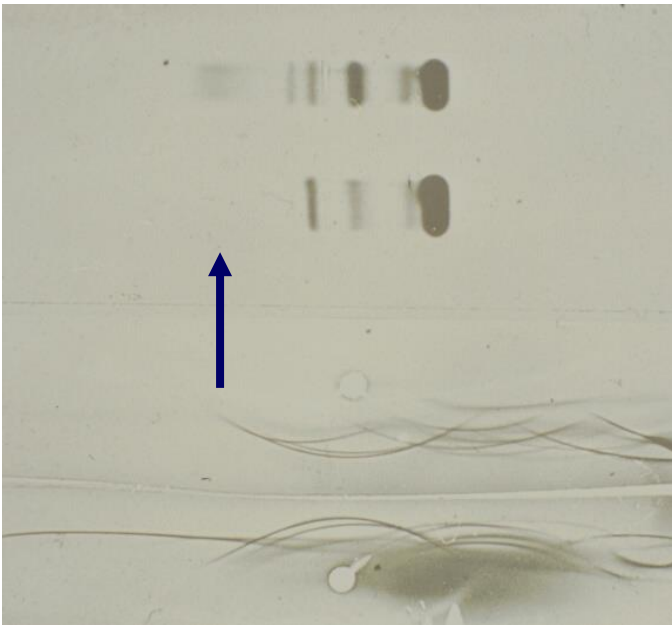


Immunoglobulines: structure

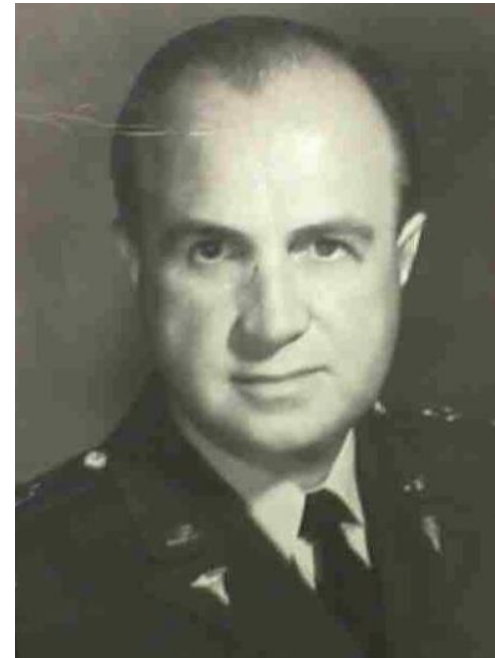


Immunoglobulin deficiency

Description of a young boy who suffered 19 episodes of clinical sepsis over 4.5 years. Pneumococcus was isolated on 10 occasions.



Bruton OC. Agammaglobulinaemia. Pediatrics. 1952

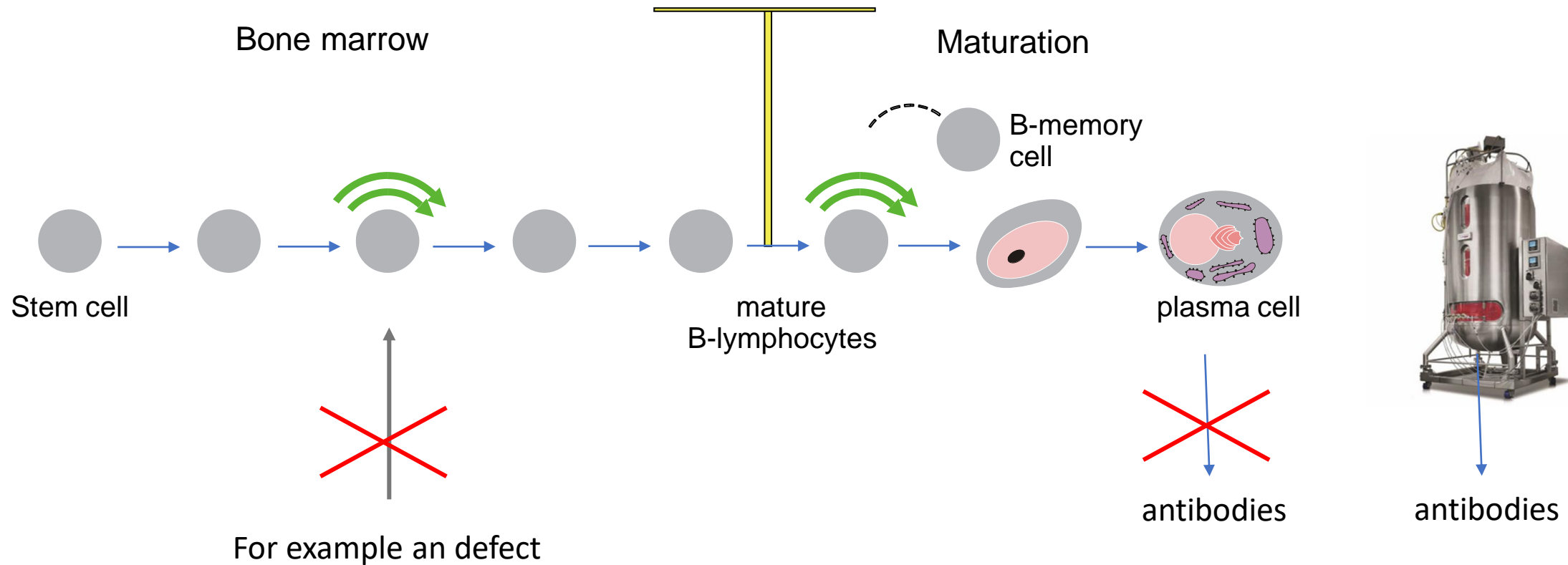


Ogden Carr Bruton



So its 70 years ago!

Defects in immunoglobulin synthesis

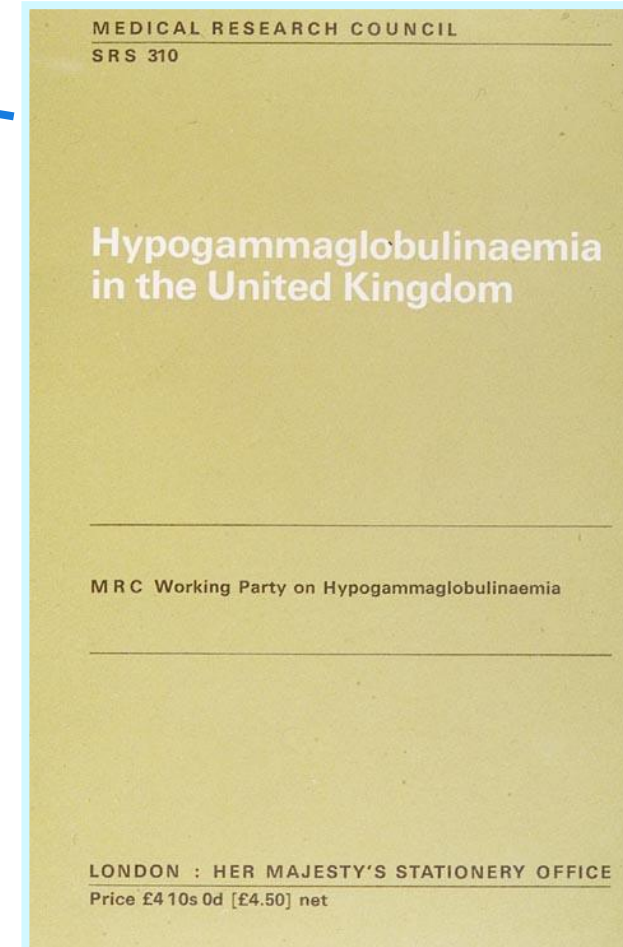


Efficacy data for Immunoglobulin therapy

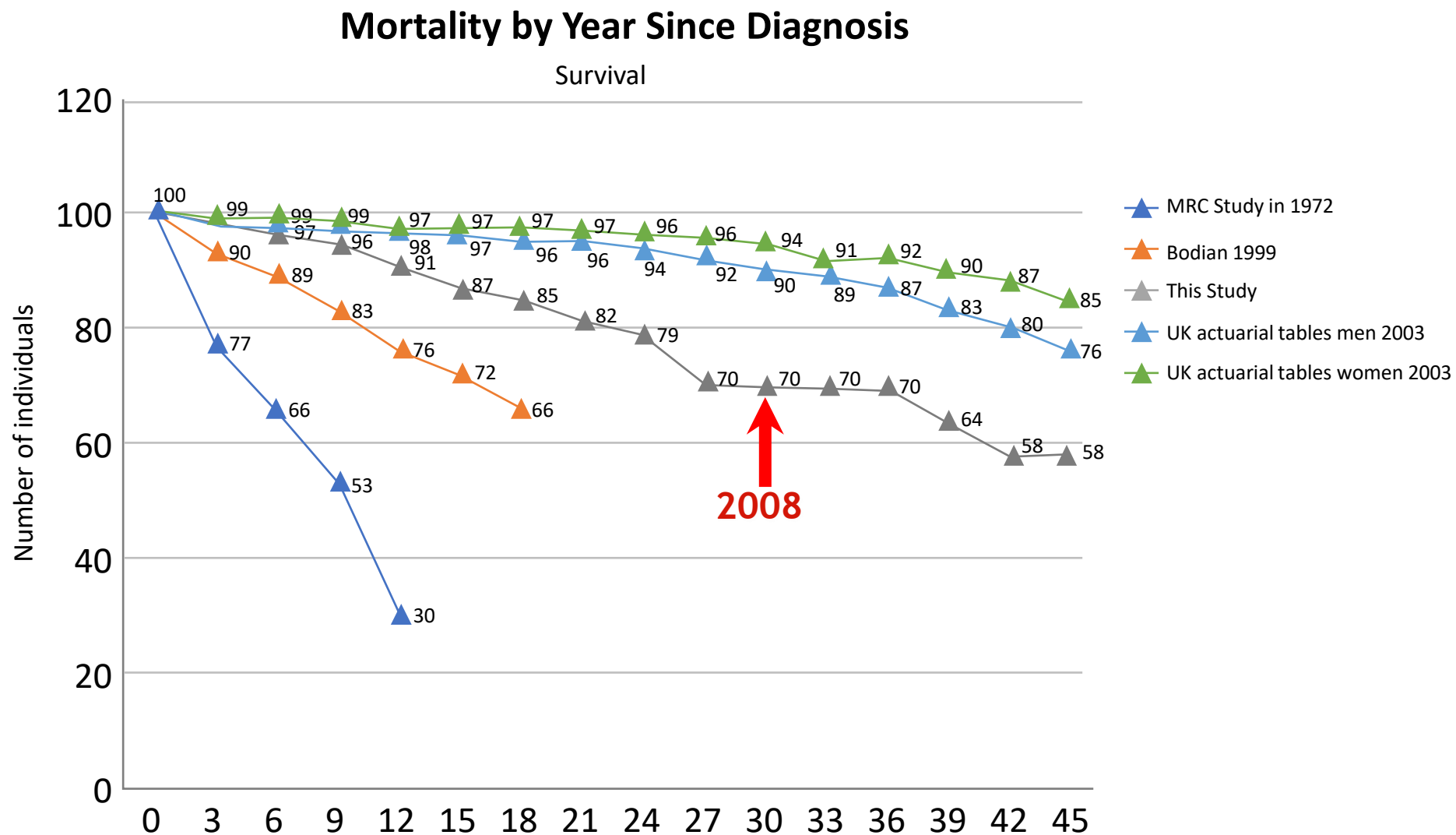
- Placebo RCT are unethical since 1971 MRC trial

Cochrane review in progress

- Outcome measures:
 - *primary* – frequency of infections
 - *secondary*- days of antibiotics, days off work/school, severity of infections



Mortality rate of CVID patients from 1972 to 2003

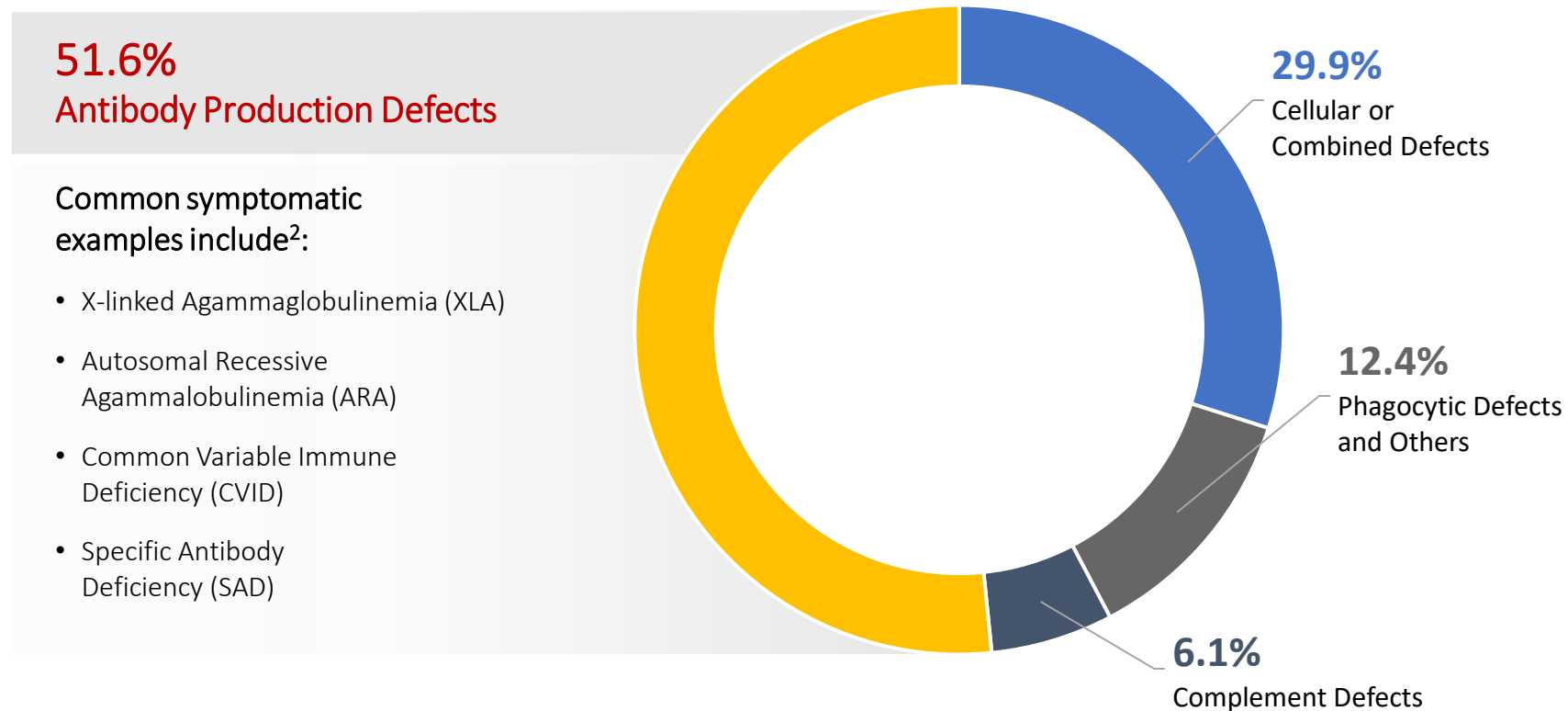


• 1. Chapel H. *Blood*. 2008.

• 2. Cunningham-Rundles C, Bodian C. *Clin Immunol*. 1999.

Antibody Production Defects are the Most Common Form of PID

- Major categories of PI from the global Jeffrey Modell Centers Network (JMCN) survey¹



Adapted from Modell 2011.

1. Modell 2011. 2. IDF Pt family handbook.

History of Ig Therapy Options



Ogden Carr Bruton

1952

First Ig Administration

By Col. Ogden Bruton in an 8-year-old boy via SC route to facilitate Ig administration¹

2013

Hyaluronidase-facilitated IGSC (HyQvia) Infusion

Introduced use of rHuPH20 to enhance the dispersion and absorption of Ig 10%³

**20....
And??**

1950

1960

1970

1980

1990

2000

2010

1950s–1970s Intramuscular (IGIM) Administration

Painful and associated with systemic reactions in a large group of patients²

1980s IGIV Administration

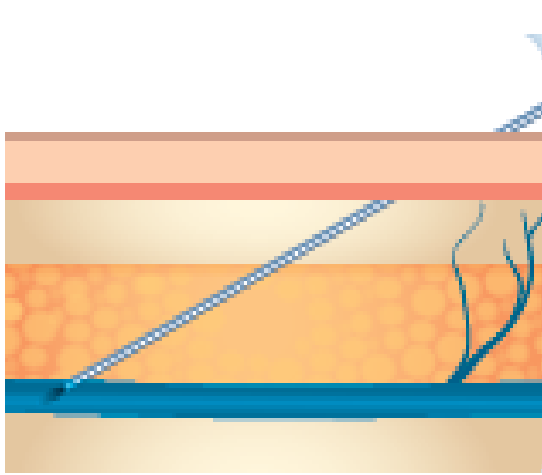
Became the most common route of administration with improved Ig purification processes that reduced ADRs²

1990s IGSC Administration

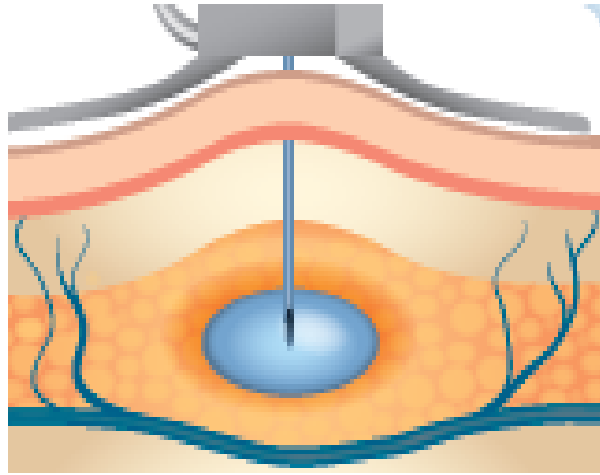
Re-emerged with the development of more concentrated Ig products²

1. Bruton OC. *Pediatrics*. 1952;9:722-729. 2. Jolles S. *Immunotargets Ther*. 2013;2:125-133.
3. Wasserman RL, et al. *J Allergy Clin Immunol*. 2012;130(4):951-957.

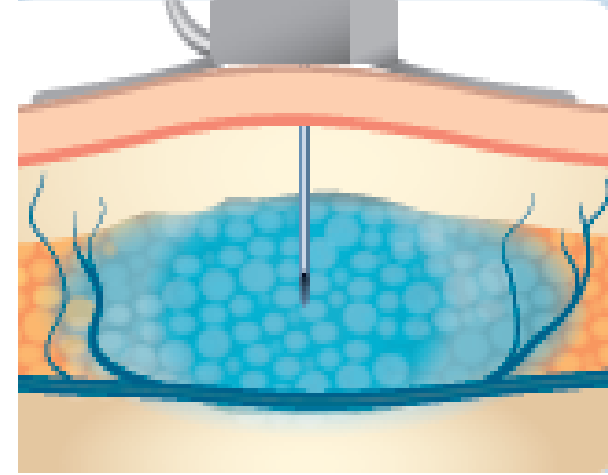
Immunoglobulin substitution therapy: 3 administration routes



Intravenous
IVIg



Subcutaneous
SCIg



Facilitated
subcutaneous fSCIg

No significant preference between the three different routes with regard to infection control.

Fascilitated IgG Infusion Experience



- 400 mL of HyQvia was infused in 2 infusion sites
- In the pivotal trial for HyQvia, infusion-site swelling generally resolved within 1-3 days

3 effective Ig options

Attribute	IVIg	Conventional SCIG	Facilitated SCIG
Infusion sites month	1	Multiple ^{2*}	Typically 1 ^{3†}
Frequency of infusions	Every 3-4 weeks ¹	Daily to every 2 weeks ¹	Every 2, 3, or 4 weeks ³
Most common ARs	Systemic reactions ²	Local site reactions ²	Local site reactions ³
Ig peak level [§]	Higher than SCIG ²	Lower than IVIg ²	Higher than SCIG but lower than IVIg ³
Administration	HCP administration ² Venous access required ²	Self-administration ^{2‡} No venous access required ²	HCP administration OR Self-administration ^{3¶} No venous access required ³

*In a study with immune globulin infusion 10% (Human) a median of 21.43 sites were required each month.

†Requires appropriate training and presence of caregiver.

§See slide 37 for details

‡Adjust the frequency and number of infusion sites, taking into consideration volume, total infusion time, and tolerability.

¶After appropriate training.



With permission from iStock



With permission from patient

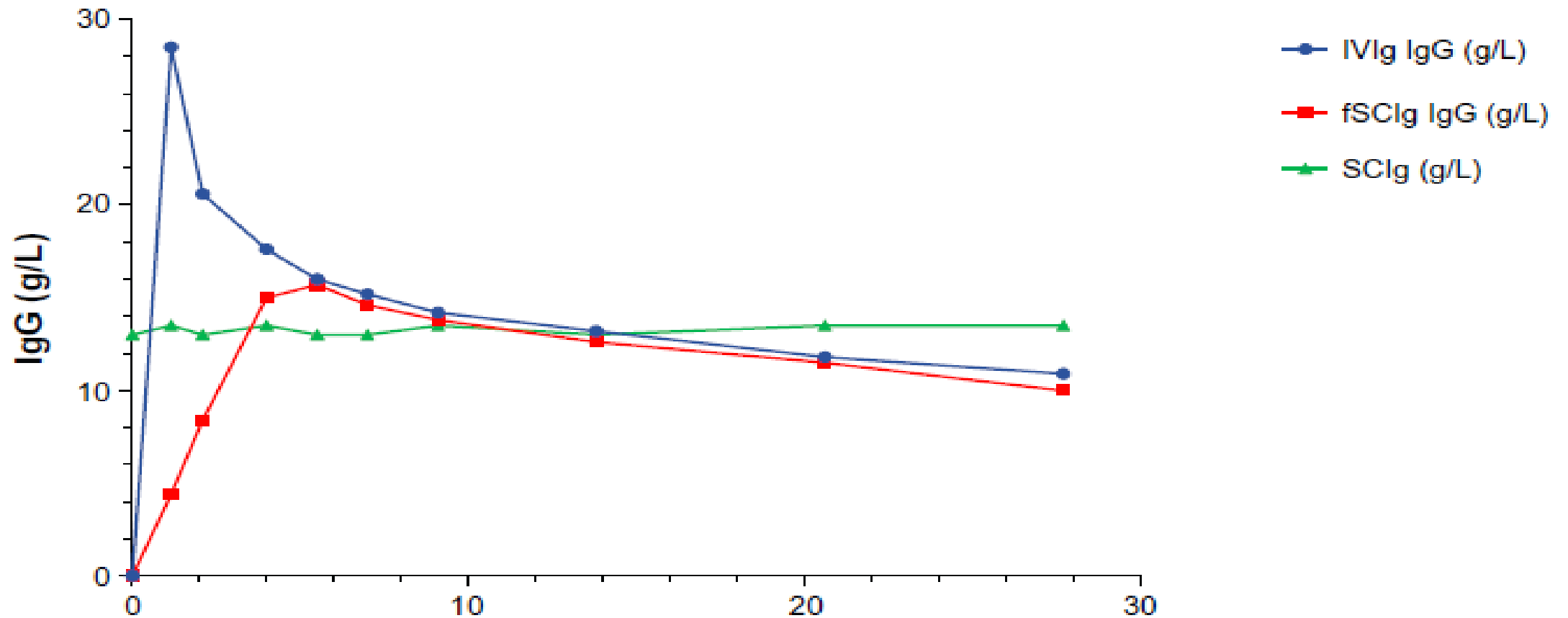


With permission from Dr. Schiff

AR=adverse reaction; HCP=healthcare professional; IVIg=intravenously administered immunoglobulin; SCIG=subcutaneously administered immunoglobulin.

1. Wasserman RL. *Immunotherapy*. 2014;6(5):553-567. 2. Wasserman RL, et al. *J Allergy Clin Immunol*. 2012;130(4):951-957. 3. HyQvia Summary of Product Characteristics. Last updated August 2016. <http://www.ema.europa.eu>.

Immunoglobulin pharmacokinetics



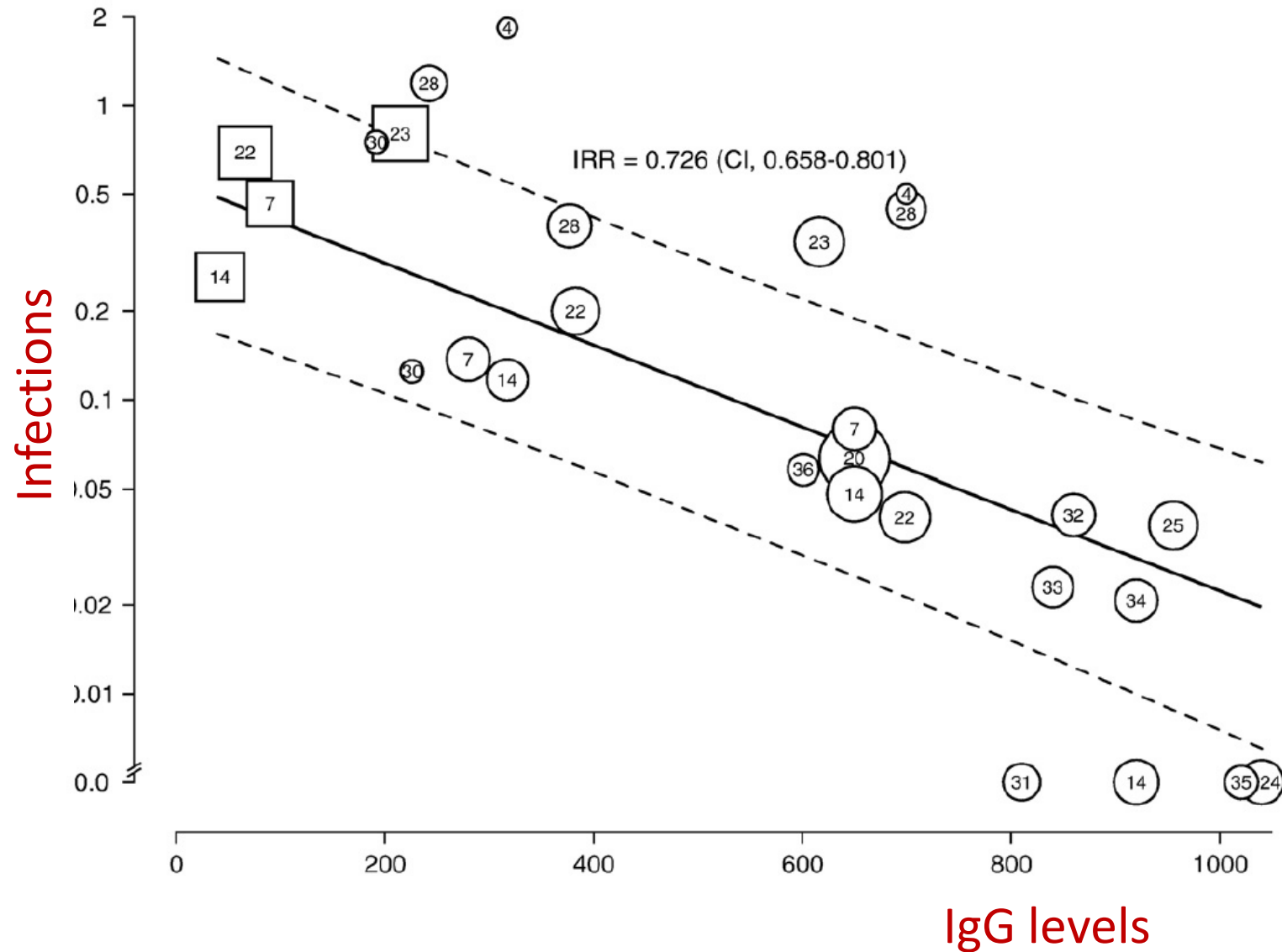
Infections

Ivlg versus ScIg versus fScIg

Equally effective in prevention of

- Overall infections
 - Severe infections
-

Higher IgG levels: less infections



Frequency and Types of Adverse Reactions (Number of Patients)

Type of reaction	IVIg [684]	SCIg [1222]
Mild: not requiring therapy		
Pain at application site	0	35
Erythema at site	0	71
Headache	15	2
Fatigue	13	2
Rigors, minor	7	24
Hot flushes	3	2
Urticaria-pruritis-eczema	3	7
Increase in pulse rate	2	1
Dizziness	1	2
Nausea	1	2
Others ^b	4	3

Major Advantages and Disadvantages of Subcutaneous and Intravenous Routes of IgG Replacement

Subcutaneous (SCIg)

Advantages

- (1) Lack of requirement for venous access.
- (2) Slow administration or gradual adsorption obviates rapid large swing in serum IgG and reduces severe headaches and other systemic adverse effects.
- (3) Maintenance of more consistent IgG levels eliminates low troughs.
- (4) Facilitates self or home infusion, increasing patient autonomy may improve patient's self-image and sense of control.

Disadvantages

- (1) Relatively small volume per infusion this requires frequent dosing--at least once a week in most cases
- (2) Ability to self-infuse requires reliable patients.

Adapted from Berger M. *Clin Immunol.* 2004.

Intravenous (IVIg)

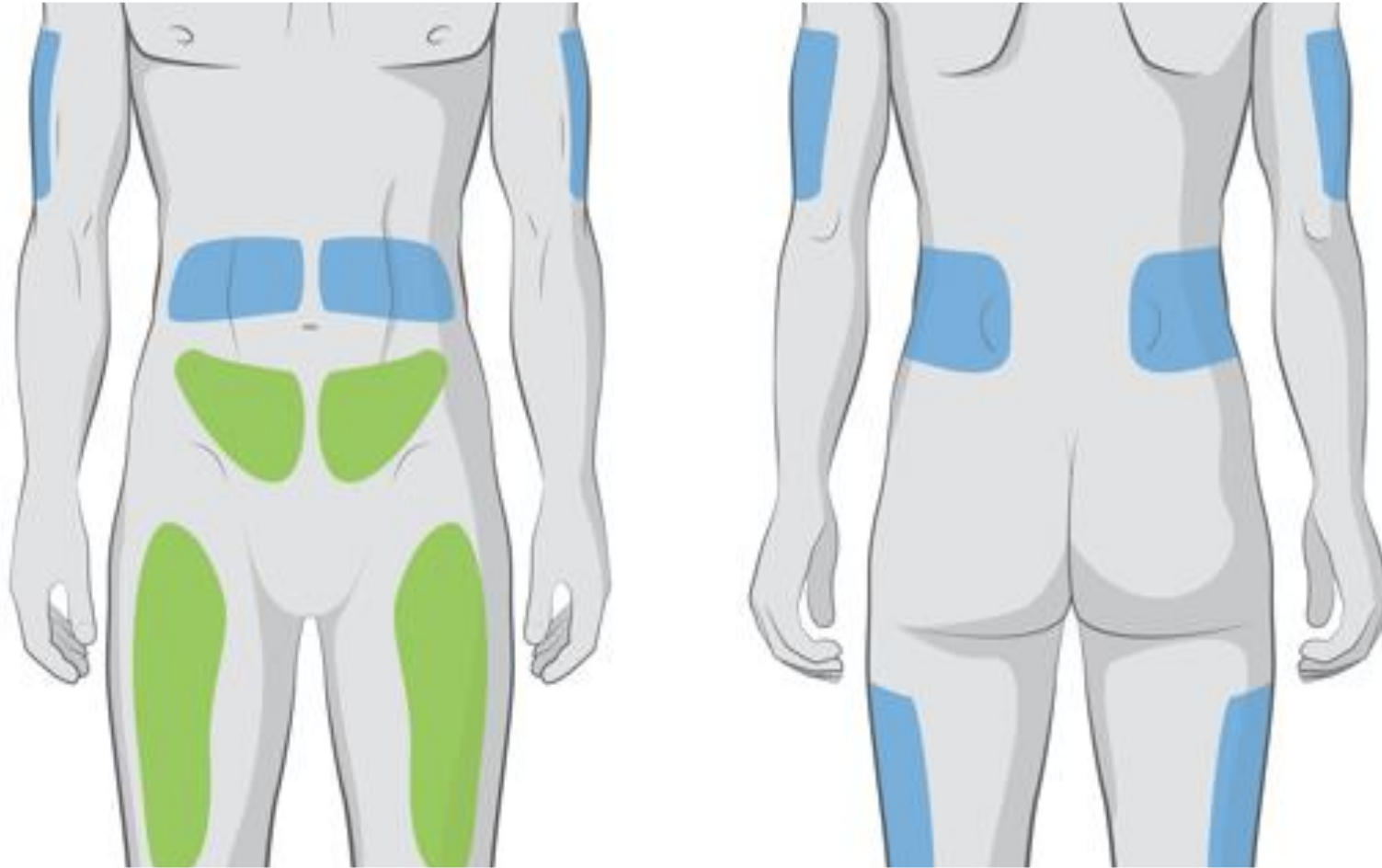
Advantages

- (1) Well tolerated by most patients.
- (2) Ability to give large volume per infusion allows intermittent dosing (every 21-28 days).

Disadvantages

- (1) Requires venous access and trained personnel in most situations.
- (2) Large shift in IgG levels during dosing interval may cause systemic adverse effects at or just after peak, and during low trough.

Infusion sites SCIg and *facilitated* SCIg (fSCIg)



fSCIg: green preferred infusion sites. Alternatives: blue

IvIg & SCIg – life style considerations

- Immunoglobulin therapy
- Personalizing IgG therapy
- The future
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Patient-tailored treatment with a focus on individual outcomes

- The dose
- Brand
- Route of administration
- Frequency and rate of infusion
- Location of administration (home or infusion center)
- Selection of a self- or health professional-administered infusion

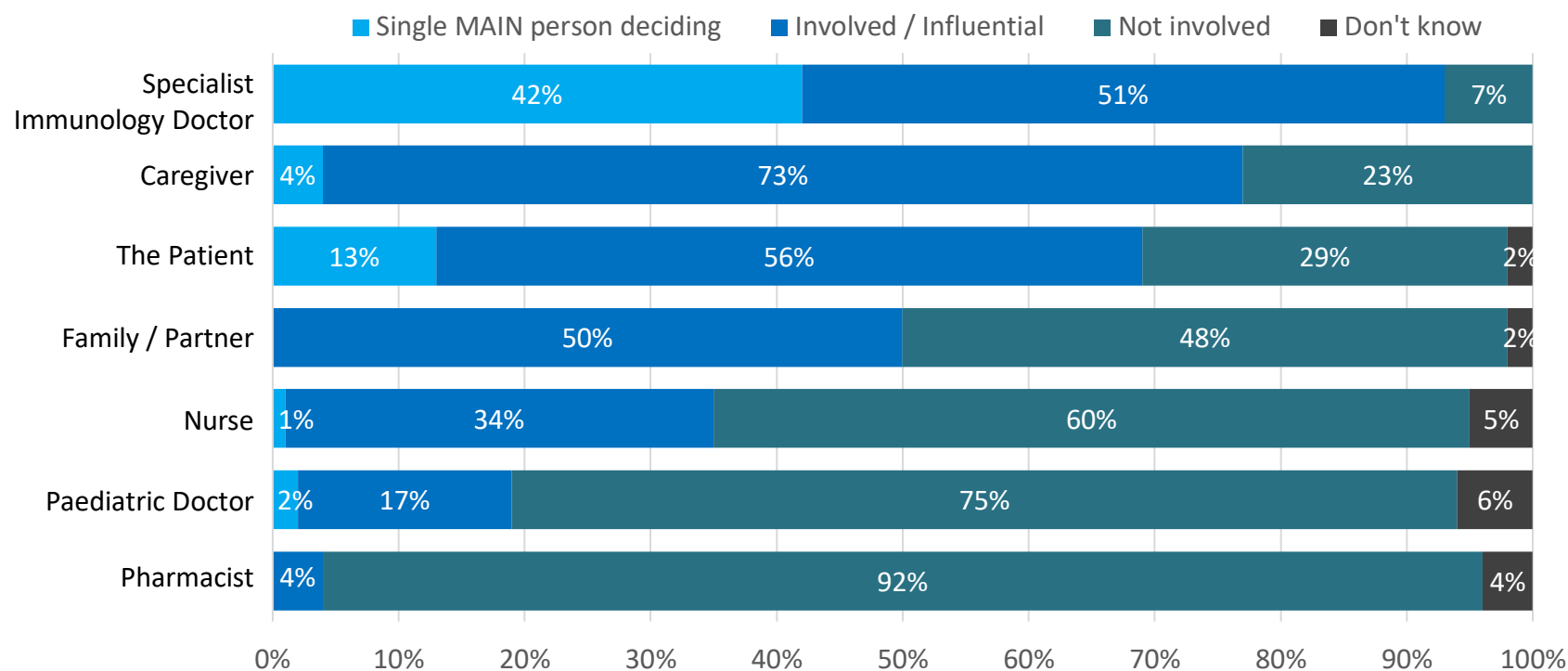
Factors That Are Important to Patients



US survey by IDF on IVIG or SCIG treatment changes substantially with age:

- 18-24 years old patients (64%) mainly use SCIG
- 25 and 54 years of age almost equally both routes
- >55 years and older predominantly use IVIG
- Other life changes, such as pregnancy, motherhood, and old age should also be considered.

Decision Makers for Route of Administration



42% of the immunology specialists are the main decision makers

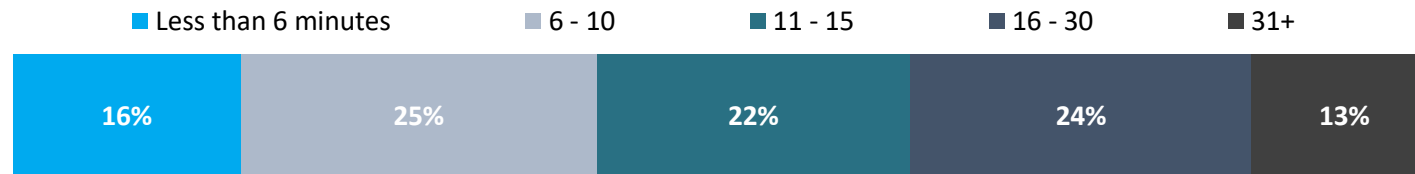
70% of patients and 77% of caregivers were involved in the decision-making process

Travel Time to Infusion and Duration of Therapy; SClg

SubC patients: How long does it take to...

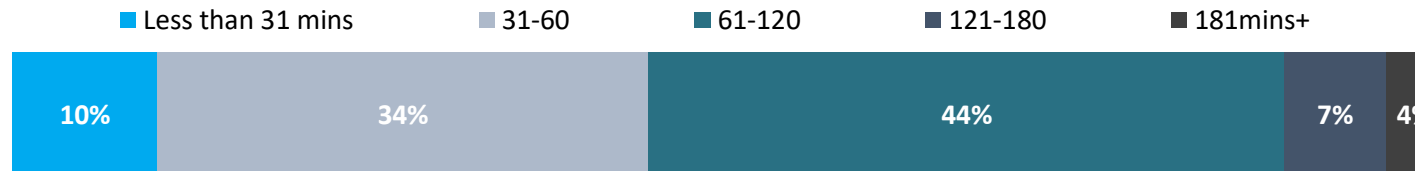
Set up the infusion equipment (including preparation of the injection site)

Average time



19 min

Carry out the infusion part of the process



1.5 hours

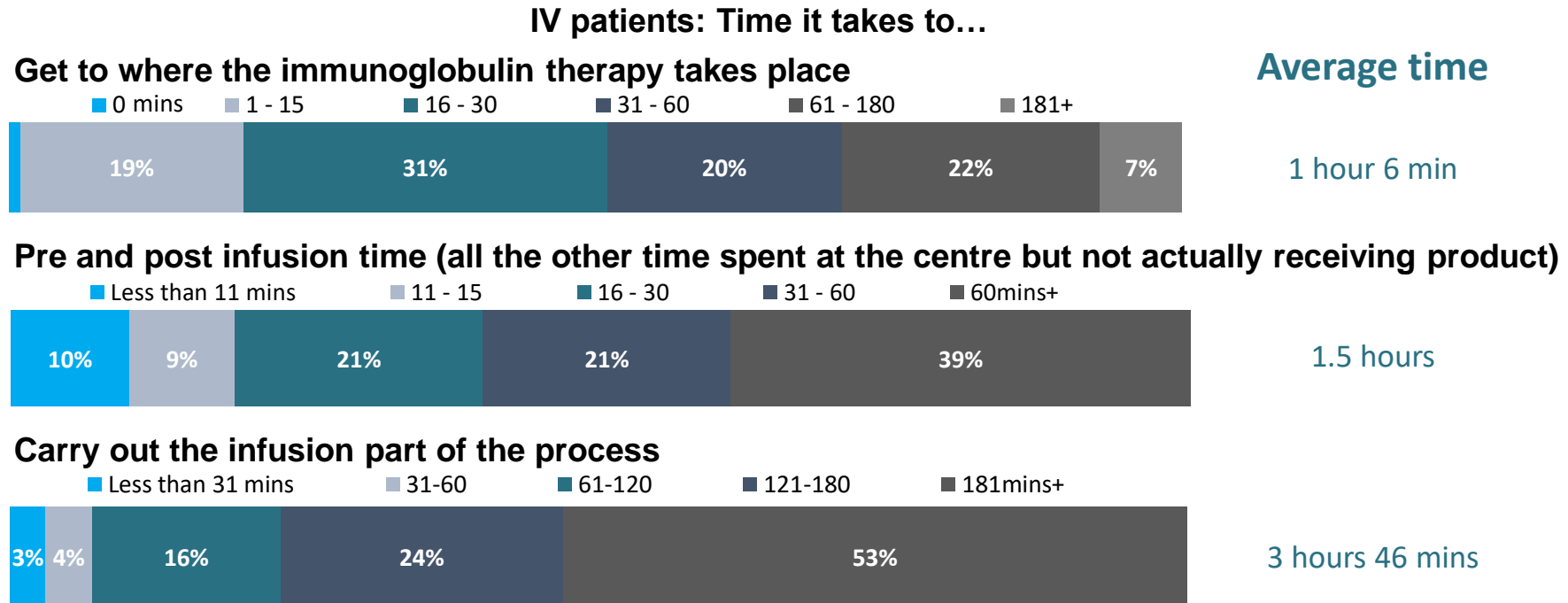
Subcutaneous patients

Takes less than 20 min on average to set up the infusion equipment

1.5 hours to complete the infusion part

Average overall time for one session is under 2 hours

Travel Time to Infusion and Duration of Therapy; IVIg



For patients on intravenous administration:

About an hour on average to get to the place of therapy

Takes 3 and a half hours to carry out the infusion part of the process

Overall time to complete treatment is over 6 hours.

Treatment with immunoglobulins in Rdam



~ 320 pts on IgHome

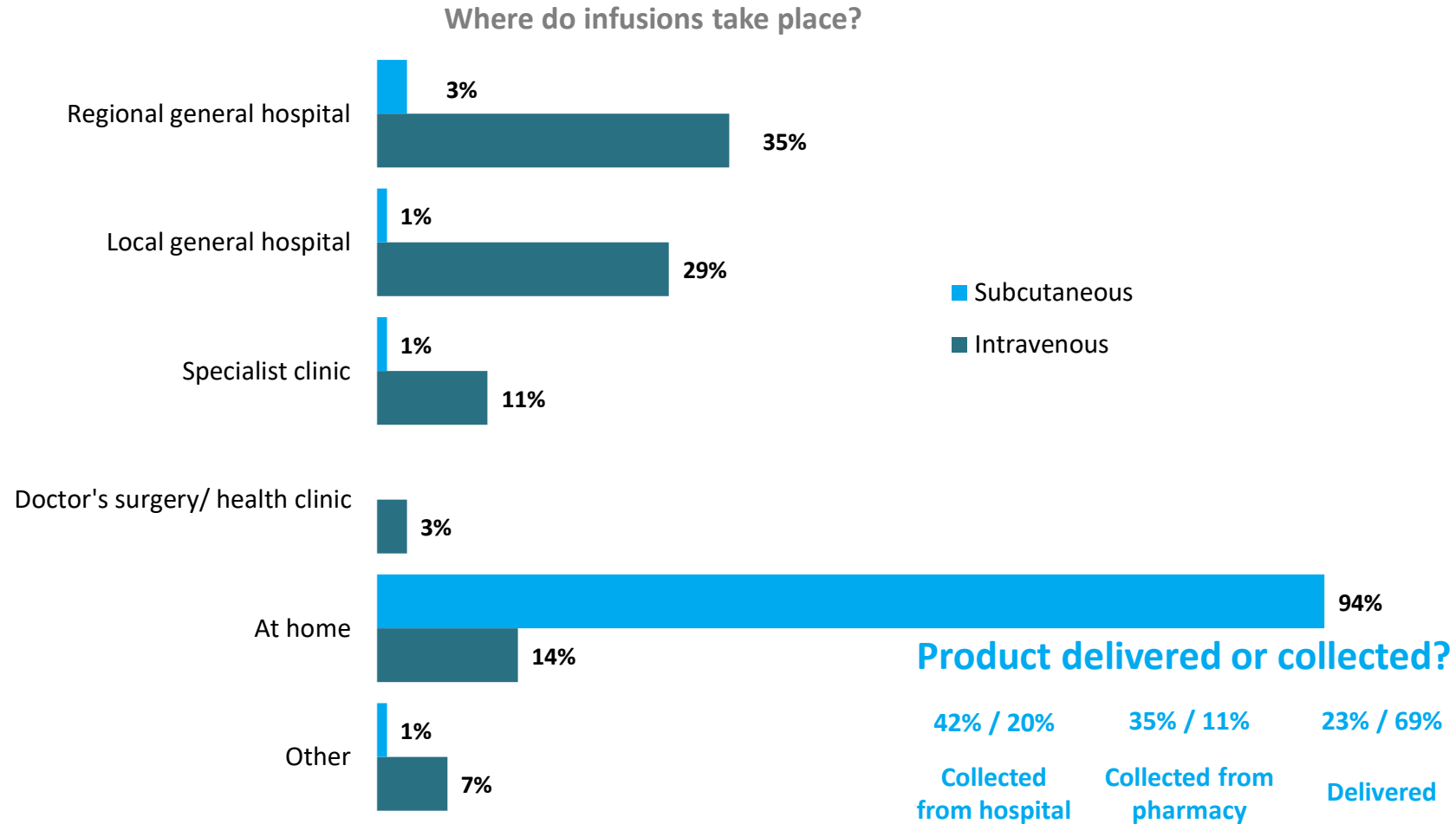
Hospital

Ivlg	~80%	>95%	<5%
ScIg	~20%	100%	0%

Specialized
home care



Treatment Location; SCIg Versus IVIg



BRYTER. IPOPI PID Patient Needs & Outlooks Survey. 2012. Available at: <http://www.ipopi.org/uploads>. Accessed 19 October 2015..

Factors That Are Important to the Doctor

Comorbidities

Venous access

Local facilities
and team



Medical indication for
choice of product

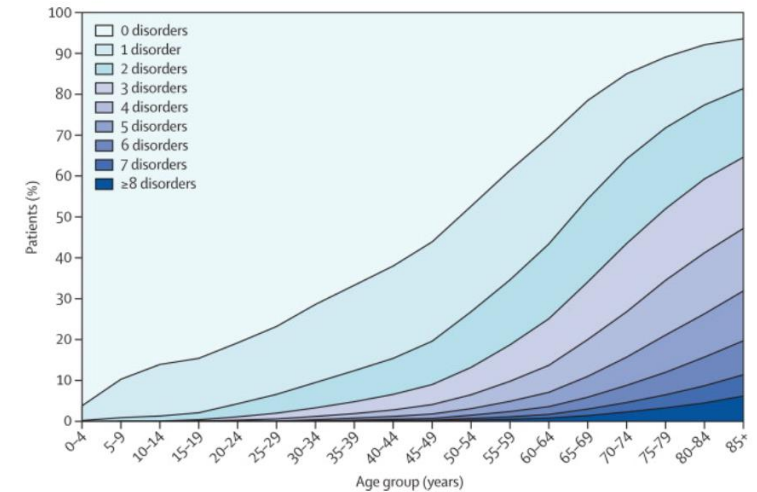
Costs

Suitability for
home therapy

What to Choose From a Doctor's Perspective

Issues

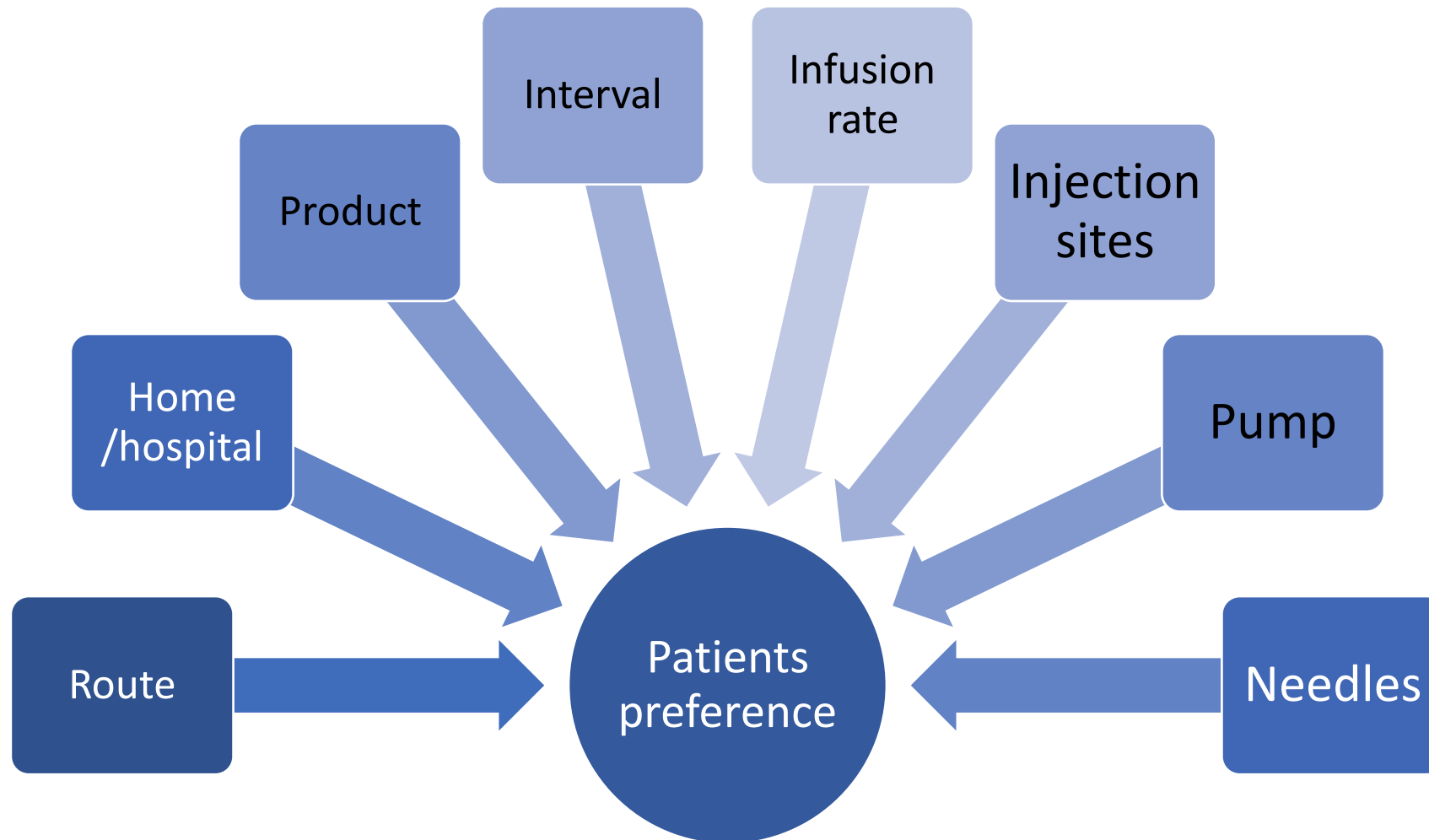
- Infusion by a professional
- Control of patients with severe complications
- Control of compliance
- Parents who have problems with SCIg substitution
- Age and comorbidities like congestive heart disease
- Skin conditions
- Platelet disorders and bleeding disorders
- Thrombosis
- Cardial and renal function
- Body composition
- Inflammatory CVID?



Barnett K et al. Lancet 2012;380:37-43.



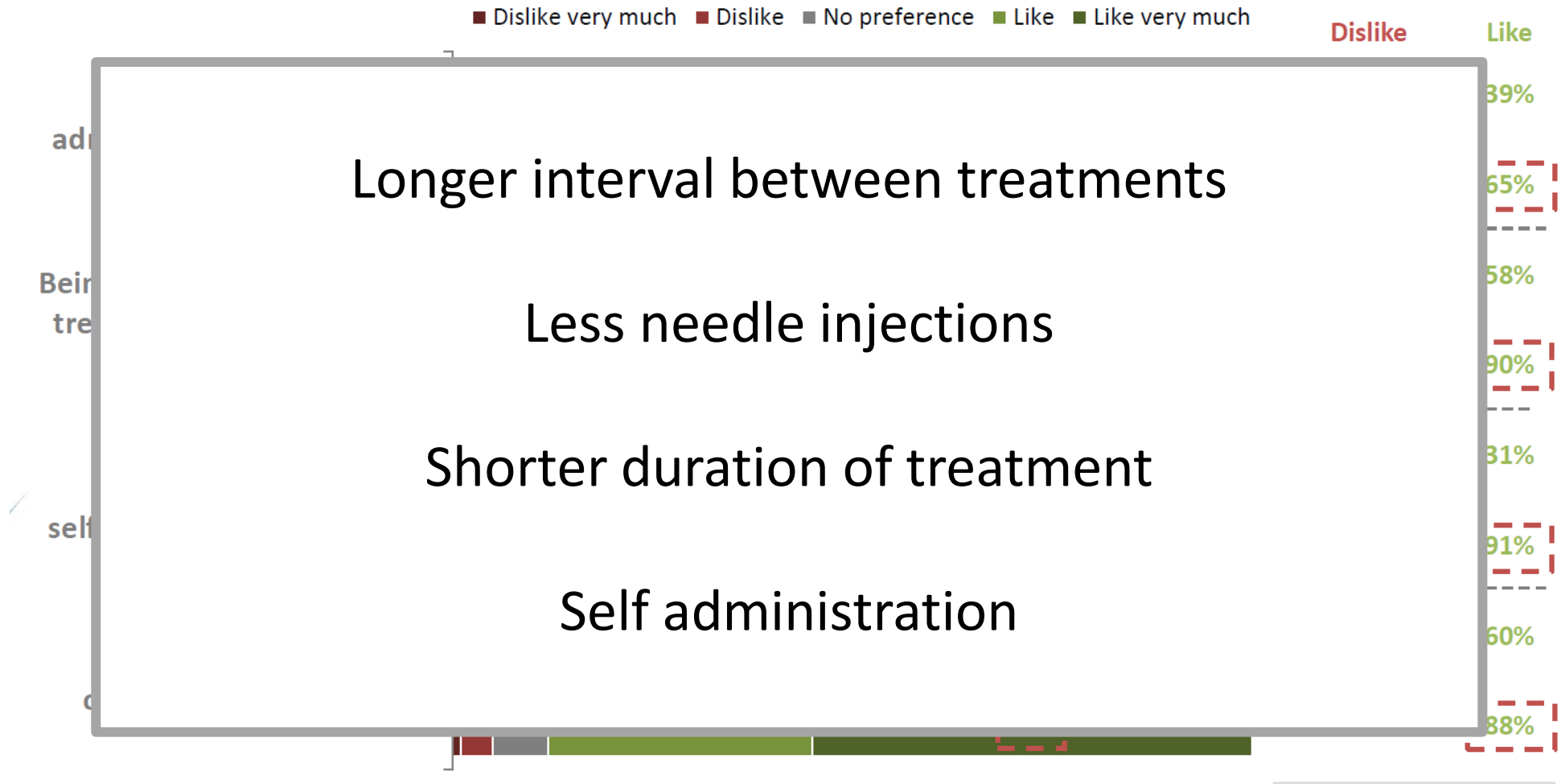
The individualised IgG therapy decision making process



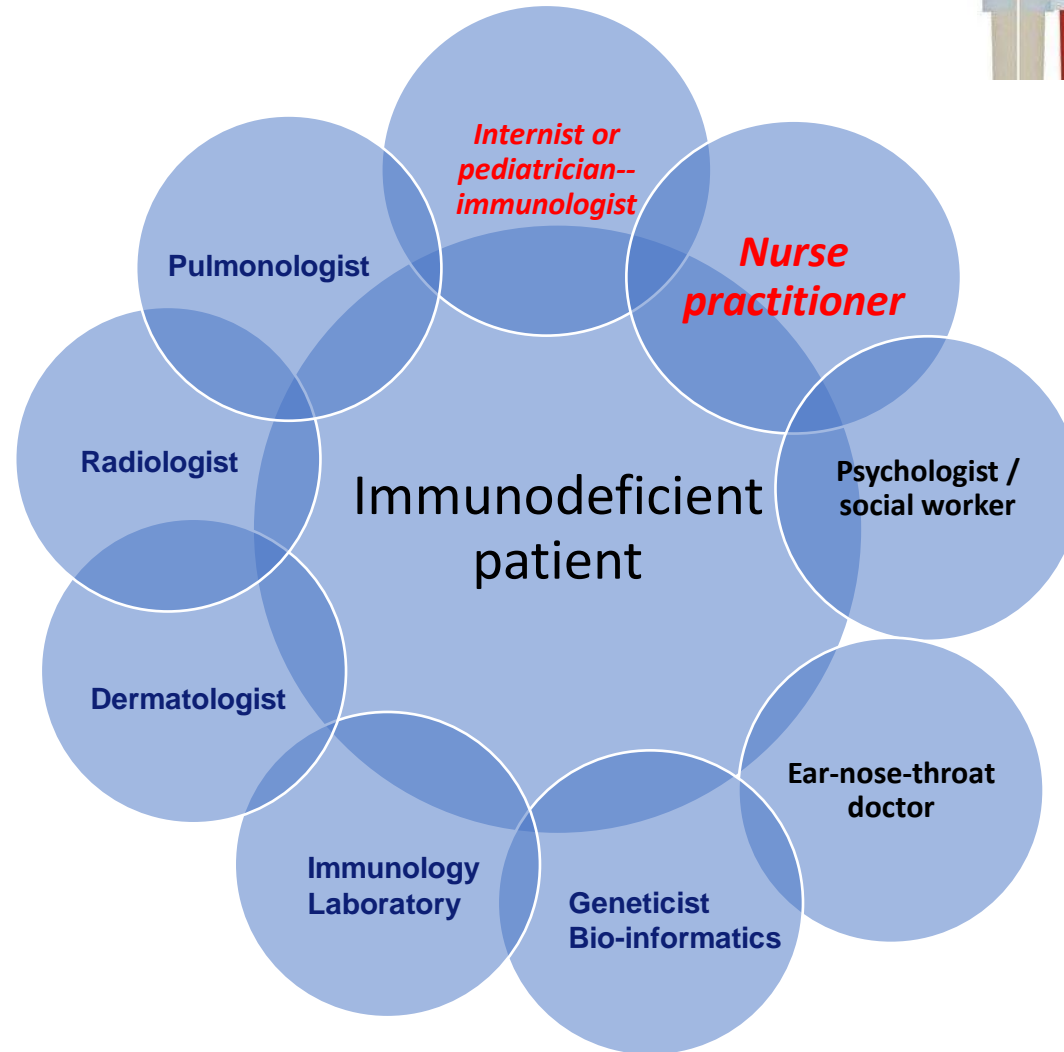
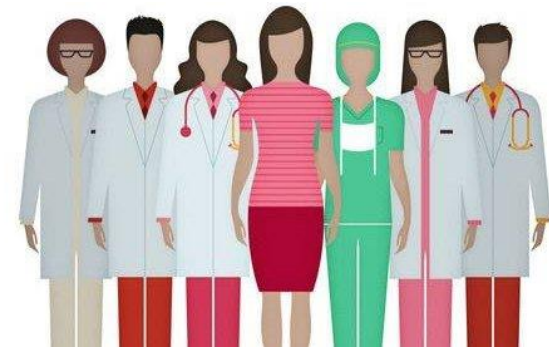
Criteria for Subcutaneous IgG (SCIg) and *facilitated* SCIg (fSCIg)

- Patient motivation
- Ability to learn and administer infusions
- Compliance
- An infusion partner who is present at the time of infusion is advisable
- A telephone must be available
- Family doctor is informed of the home therapy
- Training-program and treatment on the daycare 2 times
- Training-program 2-4 times at home care

Patient satisfaction : Ivlg versus SclG



Multidisciplinary team



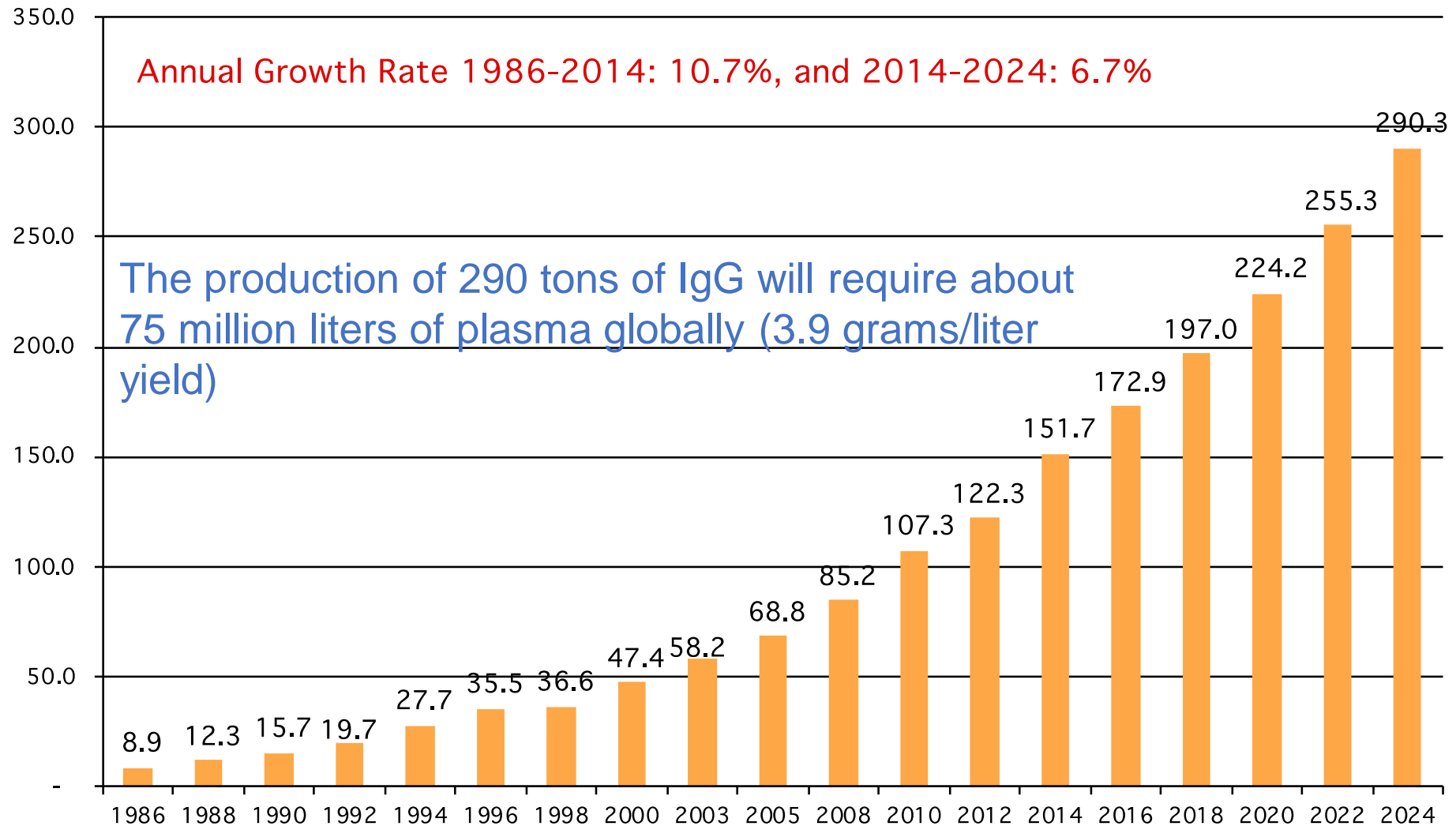
IgG replacement therapy in PIDs

- Introduction
- Immunoglobulin therapy
- Personalizing IgG therapy
- The future
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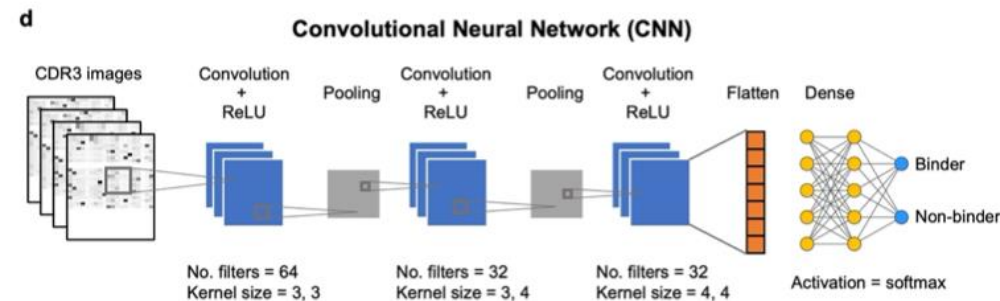
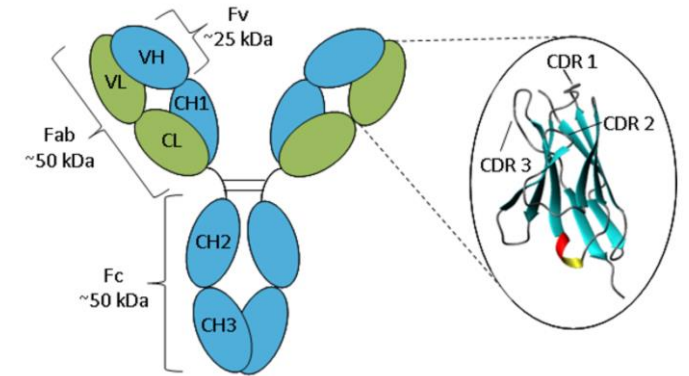
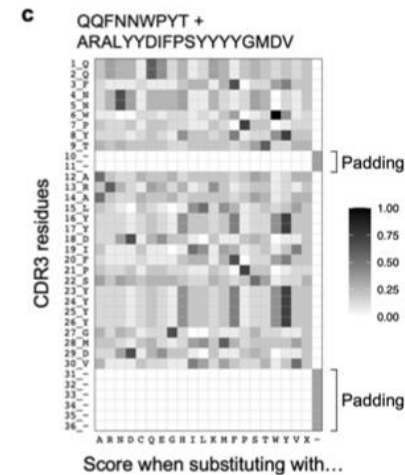
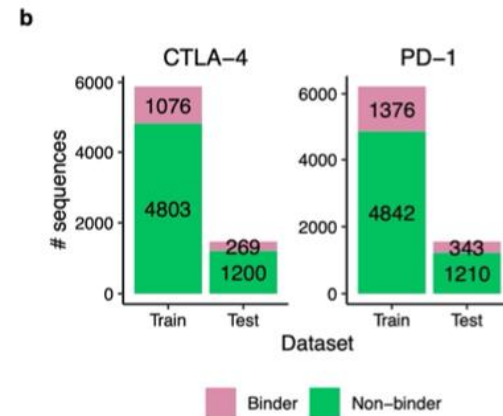
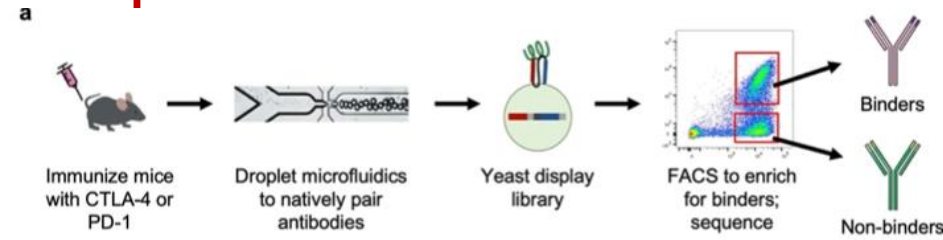
THE WORLDWIDE POLYVALENT IgG MARKET FROM 1986 TO 2024 (Metric Tons)



Highly specific IgG preparations?

- Fractionation of blood from vaccinated or donors who had a certain infection?
- Combining of global plasma pools?
- Addition of specific antibodies?

Making of certain antibodies and adding them to a preparation



IgG replacement therapy in PIDs

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In Conclusion

- Several studies have indicated that SCIg is preferred by PID patients; however this depends strongly on the individual and local situation!!!
- Burden of inflammation, psychological issues, and social aspects may be underestimated in PID.
- Personalized medicine in PID may be thought of as the tailoring of medical treatment to the individual characteristics, needs, and preferences of a patient during all stages of care (adapted from the FDA)¹

1. United States Food and Drug Administration (FDA). Paving the Way for Personalized Medicine. Available at: <http://www.fda.gov/ScienceResearch/SpecialTopics/PersonalizedMedicine/UCM372421.pdf>. Accessed 29 October 2015.

Immunodeficiency Centre Rotterdam

