Session 8: Clinical life odyssey/itinerary of PIDs

Transition from adulthood to elderly

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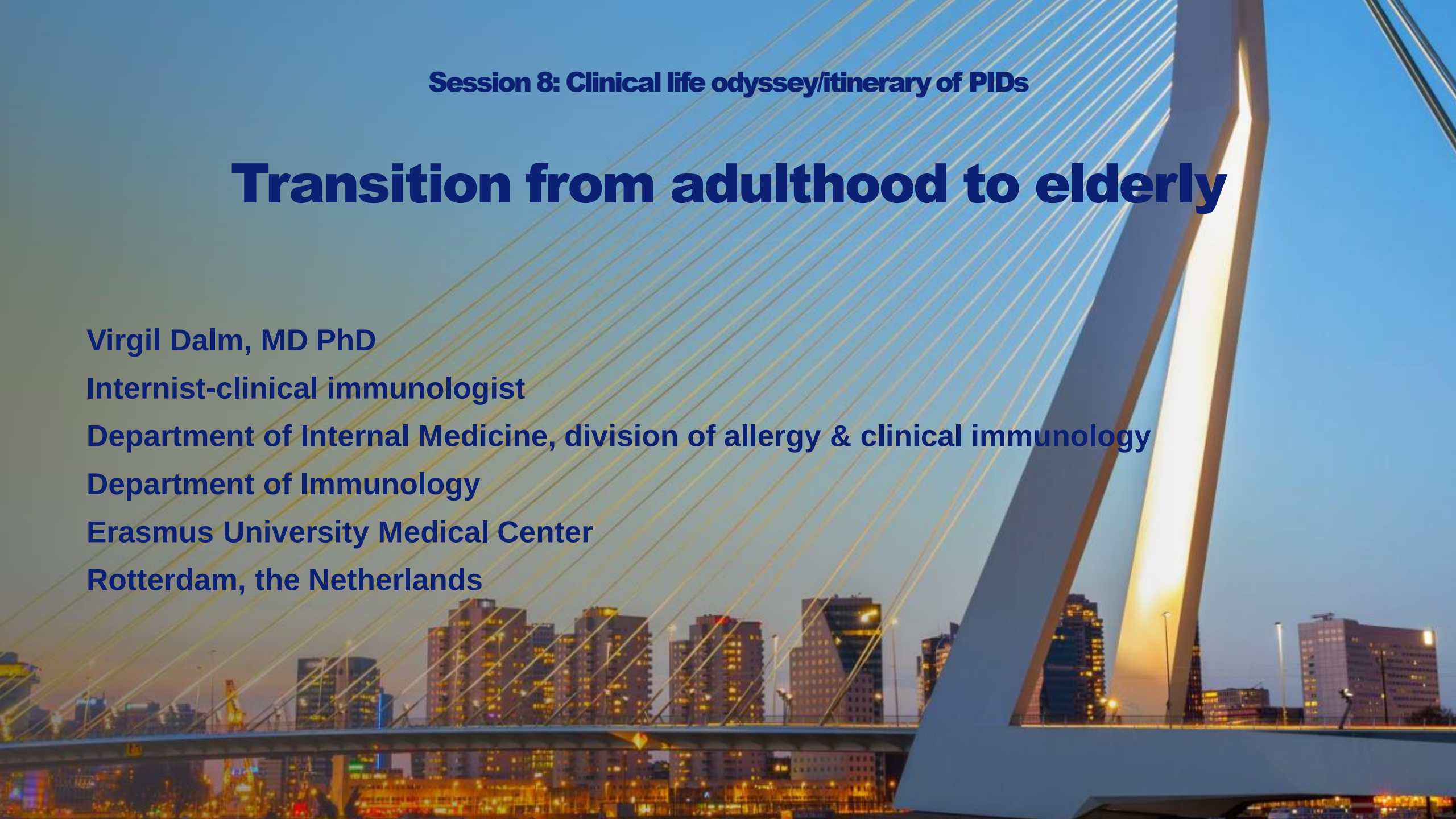

Disclosures

(Potential) conflict of interest	
Potentially relevant company relationships in connection with event	Company names
• Sponsorship or research funding	• Takeda, CSL Behring, Pharming
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• Shareholder	• None
• Other relationship, i.e. research funding	• ZonMw, Horizon 2020

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Is PID a problem in the elderly?

Is PID a problem in the elderly?

Transition from childhood to adulthood

Is PID a problem in the elderly?

Transition from childhood to adulthood to elderly population?

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An exception or an example?

In 2011 a 70-year old female patient visiting our clinics because of suspected ID

Medical history

1998	House dust mite allergy
2006	Pneumonia, admission ICU
2011 (mar)	Pneumonia, antibiotic treatment
2011 (apr)	Pneumonia, admission ICU
2011 (aug)	IgG 0.1 g/l; IgA < 0.01 g/l, IgM < 0.30 g/l

Is there a (primary) immunodeficiency?

An exception or an example?

Secondary immunodeficiency?

- No use of medication
- No signs of gastrointestinal tract and/or renal problems
- No signs of (hematological) malignancy
  No abnormalities on PET/CT scan, no signs of gynecological malignancy
  Bone marrow aspiration normal

Could it be a primary immunodeficiency?

T- and NK-cell numbers within normal limits, including T cell subsets

B-cells : undetectable numbers of memory B-cells, other subsets within normal

An exception or an example?

Diagnosis

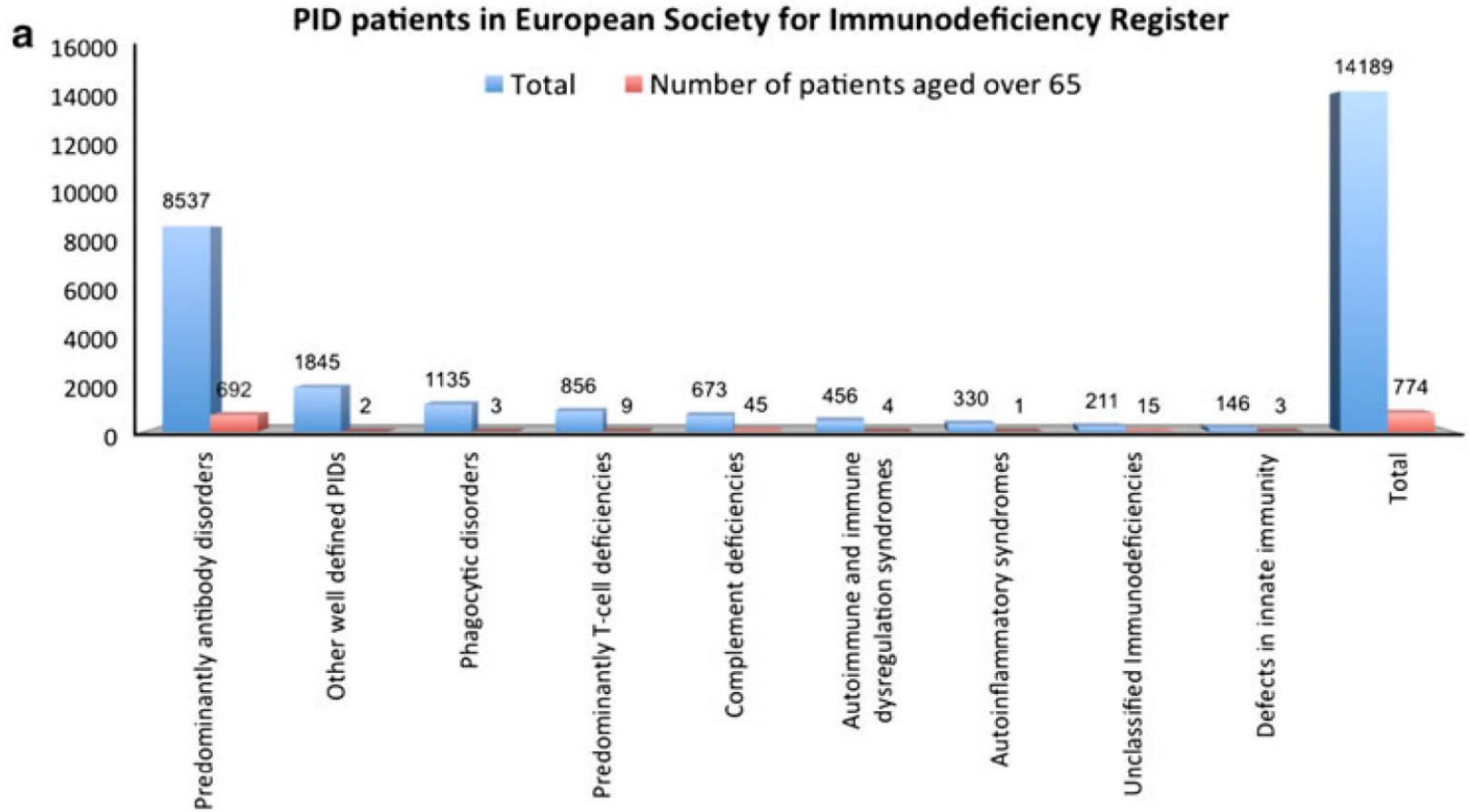
Late-onset (primary) immunodeficiency (agammaglobulinemia)

Clinical features dominated by recurrent, severe respiratory tract infections

Start immunoglobulin replacement therapy with good clinical response

PID in the elderly population

2012 : 5.5 % of ESID registered patients age > 65 years



Verma N et al. Drugs Aging 2013

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PID in the elderly population

Table 2 Patient characteristics

Characteristics	Data completeness, n (%)	
Sex, n (%)	2700 (100%)	
Male		1294 (47.9)
Female		1406 (52.1)
Age at diagnosis, years,	2700 (100%)	
Median (Min; Max)		31.0 (4; 89)
Mean (SD)		31.4 (19.6)
N (%)		
4–10		460 (17.0)
11–20		475 (17.6)
21–40		939 (34.8)
41–60		565 (21.0)
> 60		261 (9.7)

Odnoletkova I et al. Orphanet Journal of Rare Diseases 2018

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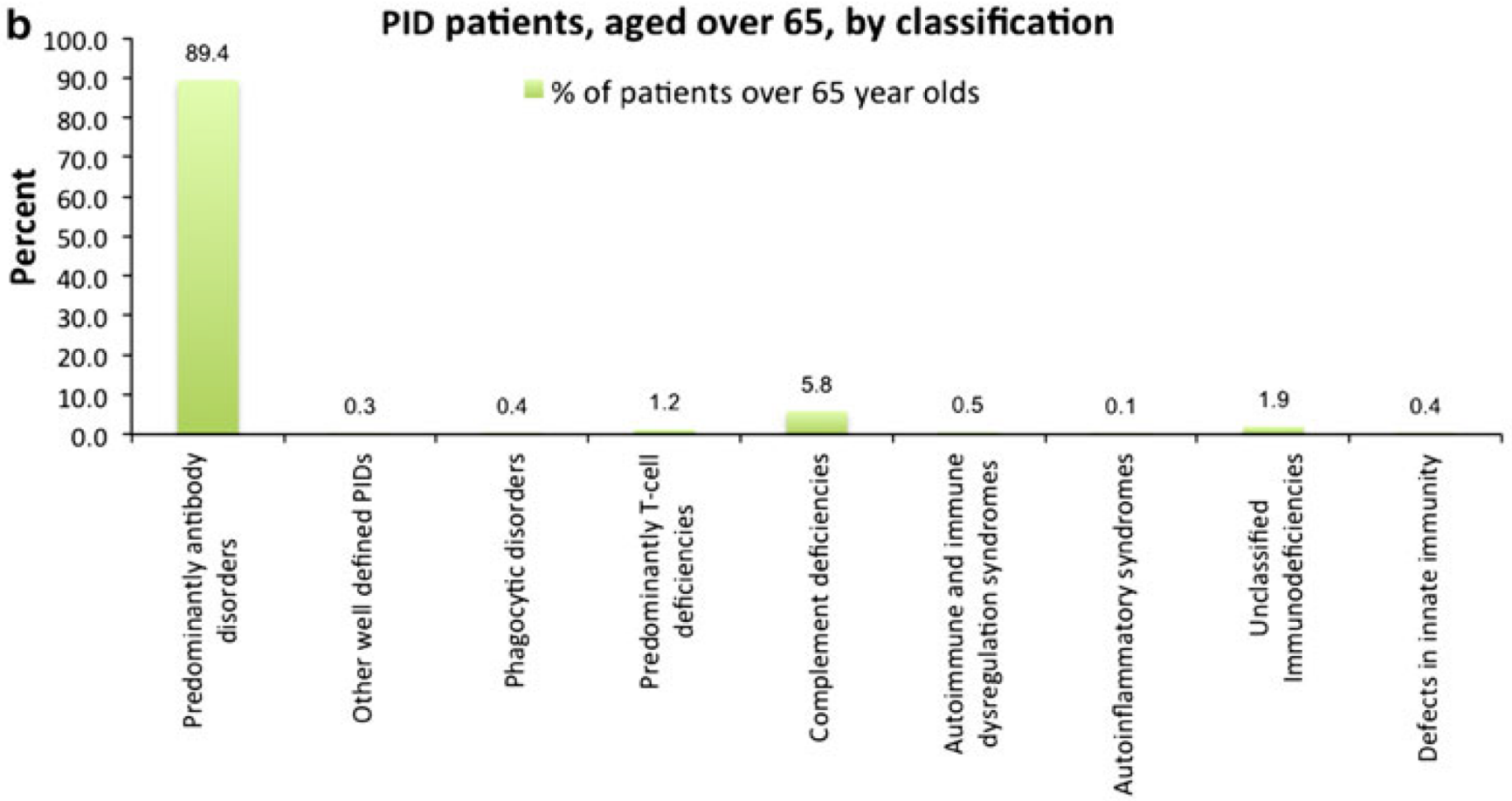
PID in the elderly population

Predominantly antibody deficiencies



Verma N et al. Drugs Aging 2013

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Is it worse in the elderly?

Potential contributing factors and points to consider

- Effects on immune system
- Non-immunological changes in physiology
- Change of treatment?
- Considerations for follow-up : other complications than in adulthood?
- What should we and what shouldn’t we do?

Effects on the immune system

The role of immunosenescence?

Protein-energy malnutrition (PEM)

High prevalence deficiencies in micronutrients (vitamin D, zinc, vitamin E)

Undernourishment:

16% of people > 65 years and 2% of people >85 years are classed as malnourished

Tannou T et al. Medecine et maladies infectieuses 2019; Ahmed T. Clin Interv Aging

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Structural changes

Structural and functional changes in skin and mucosal barriers

Table I. Morphologic changes in normal aged skin*

Epidermis	Appendages
± Slight ↓ epidermal thickness	↓ Number eccrine glands
↓ Vertical height and ↑ surface area of keratinocytes	Attenuation eccrine and apocrine glands
↓ Corneocyte adhesion	Sebaceous gland hyperplasia
↑ Cytoarchitectural disarray	↓ Number hair follicles scalp and face
Flattened dermoepidermal junction	Changes in hair shaft diameter
Reduplication lamina densa and anchoring fibril complex	Hair graying
↓ Number melanocytes	Thinning and longitudinal ridging nail plate
↓ Number Langerhans cells	↓ Nail lunula size

Subcutaneous tissue	Dermis
↓ Especially face, hands, shins, feet	Atrophy
↑ Waist (men) and thighs (women)	↓ Number fibroblasts
	↓ Number mast cells
	↓ Papillary capillary network
	Blood vessel alterations
	Abnormal nerve endings

Fenske NA et al. J Am Acad Dermatol 1986

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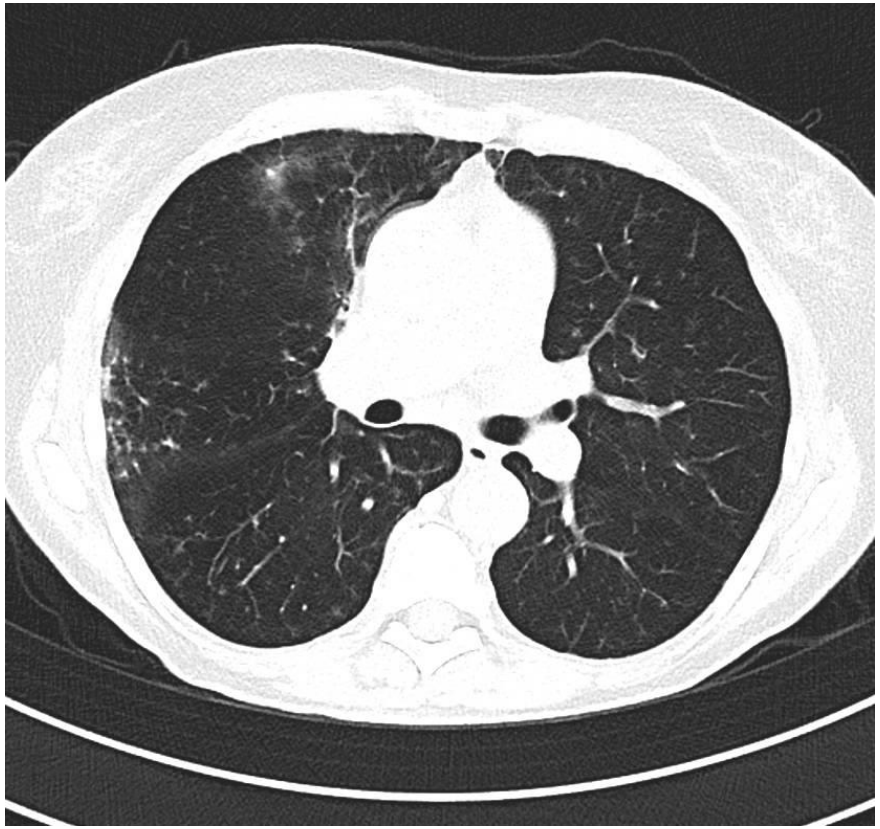
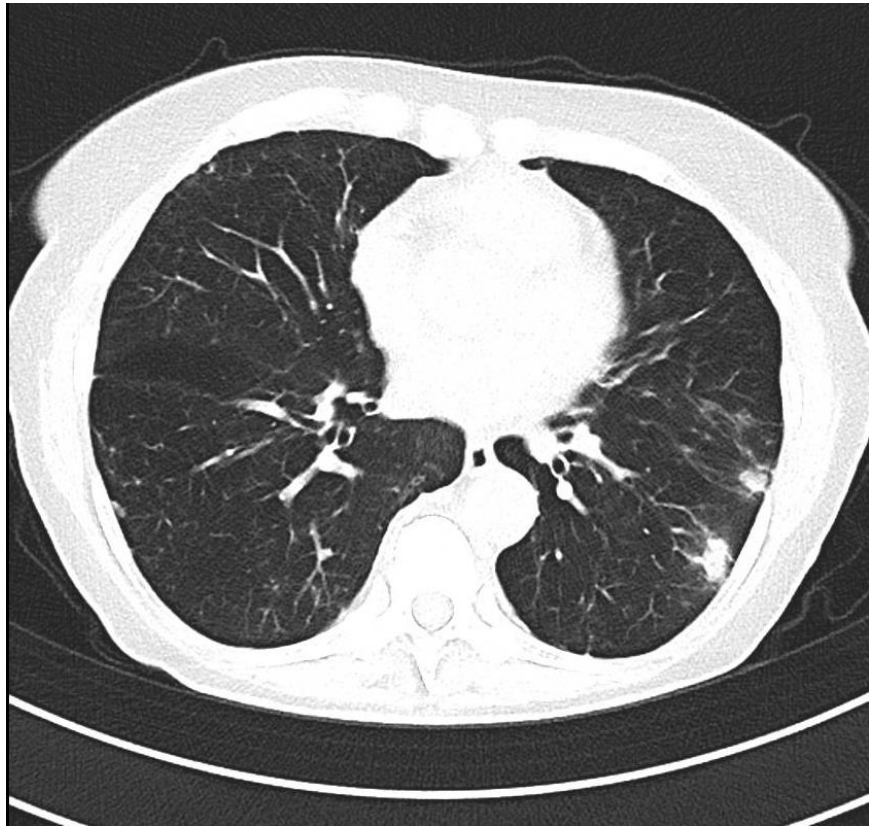
Back to our patient

CT-scan 2020 (age 79) : what to do?





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Changes in follow-up?

Table 1. Baseline characteristics in 78 younger and older CVID patients.

		<65 Years Old *n* (%)	≥65 Years Old *n* (%)
Number of Patients	Male	24 (37)	2 (15)
	Female	41 (63)	11 (85)
Age at First Clinical Presentation (Years)	Mean ± SD [1]	29 ± 18	67 ± 5
	Median	30	66
Age at Diagnosis (years)	Mean ± SD [1]	41 ± 15	70 ± 5
	Median	41	69
Diagnostic Delay (Months)	Mean ± SD [1]	139 ± 173	34 ± 41
	Median	84	36

[1] SD: standard deviation.

Danieli MG et al. Biomedicines 2022

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Changes in clinical symptoms?

More neoplasms in older patients with CVID

Table 3. Clinical phenotypes at CVID diagnosis and at last follow-up control.

	<65 Years Old *n* (%)		≥65 Years Old *n* (%)	
	Diagnosis	**Follow-Up**	**Diagnosis**	**Follow-Up**
Non-complicated (infections only)	40 (61)	21 (32)	9 (69)	5 (38)
Autoimmunity	12 (18)	29 (44)	4 (31)	5 (38)
Immune thrombocytopenic purpura	7 (10)	10 (15)	0 (0)	1 (7)
Autoimmune haemolytic anaemia	2 (3)	2 (3)	1 (7)	1 (7)
Others (autoimmune hepatitis, Devic's disease, Hashimoto's thyroiditis, IDDM, myelitis, PBC, psoriasis, psoriatic arthritis, Sjogren's syndrome, systemic sclerosis, vasculitis, vitiligo)	4 (6)	17 (26)	3 (23)	3 (23)
Polyclonal lymphoproliferation	3 (5)	13 (20)	1 (7)	2 (15)
Enteropathy	6 (9)	12 (18)	1 (7)	1 (7)
Neoplasia	4 (6)	13 (20)	1 (7)	5 (38)
LNH	2 (3)	4 (6)	1 (7)	2 (15)
Other neoplasms (stomach, pancreas, breast, skin, thyroid, LGL, bladder)	2 (3)	9 (13)	0 (0)	3 (23)

Danieli MG et al. Biomedicines 2022

Changes in clinical symptoms?

Higher number of elderly CVID patients with chronic lung disease

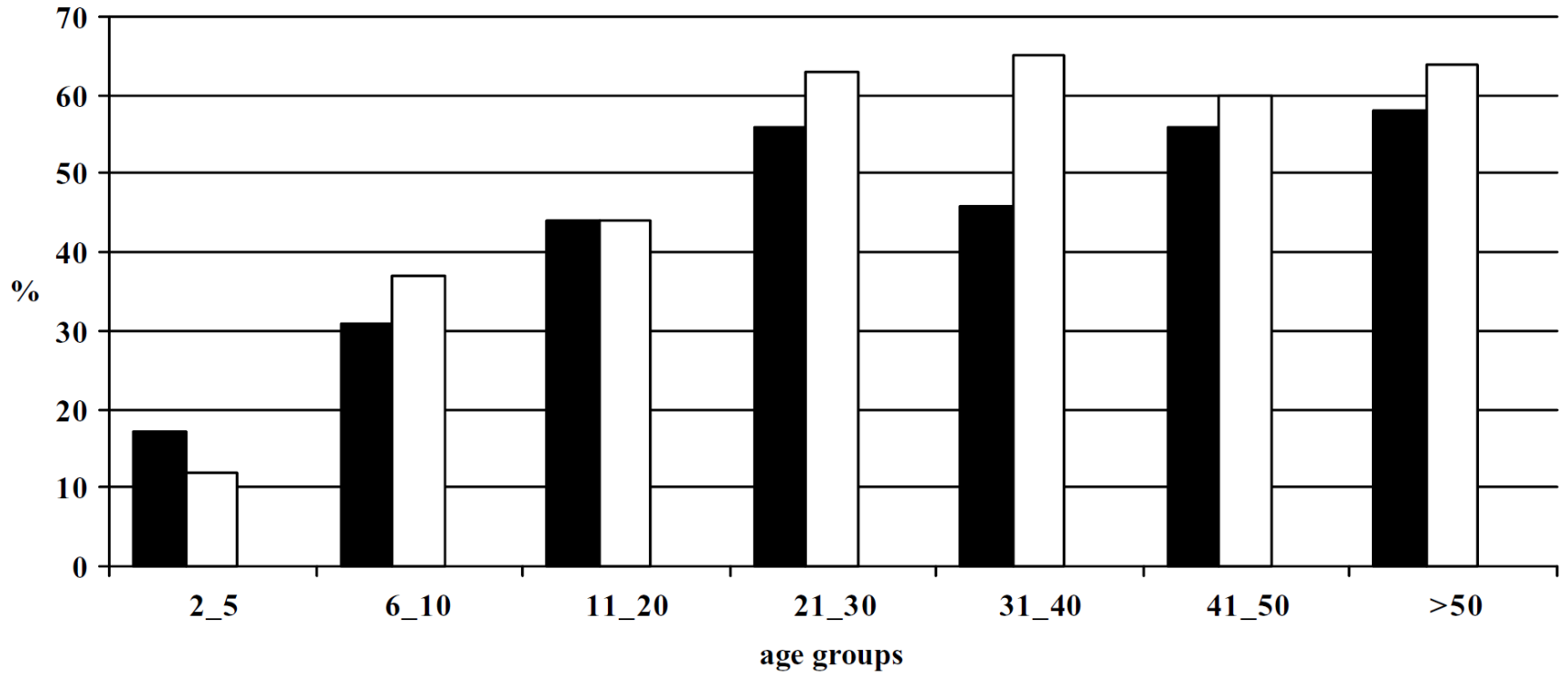

Fig. 4. Prevalence of patients with CLD at diagnosis (*black bars*) and during follow-up (*white bars*). All CVID patients enrolled in the study at the time of diagnosis were followed up and grouped in age intervals, as indicated.

Quinti I et al. J Clin Immunol 2007

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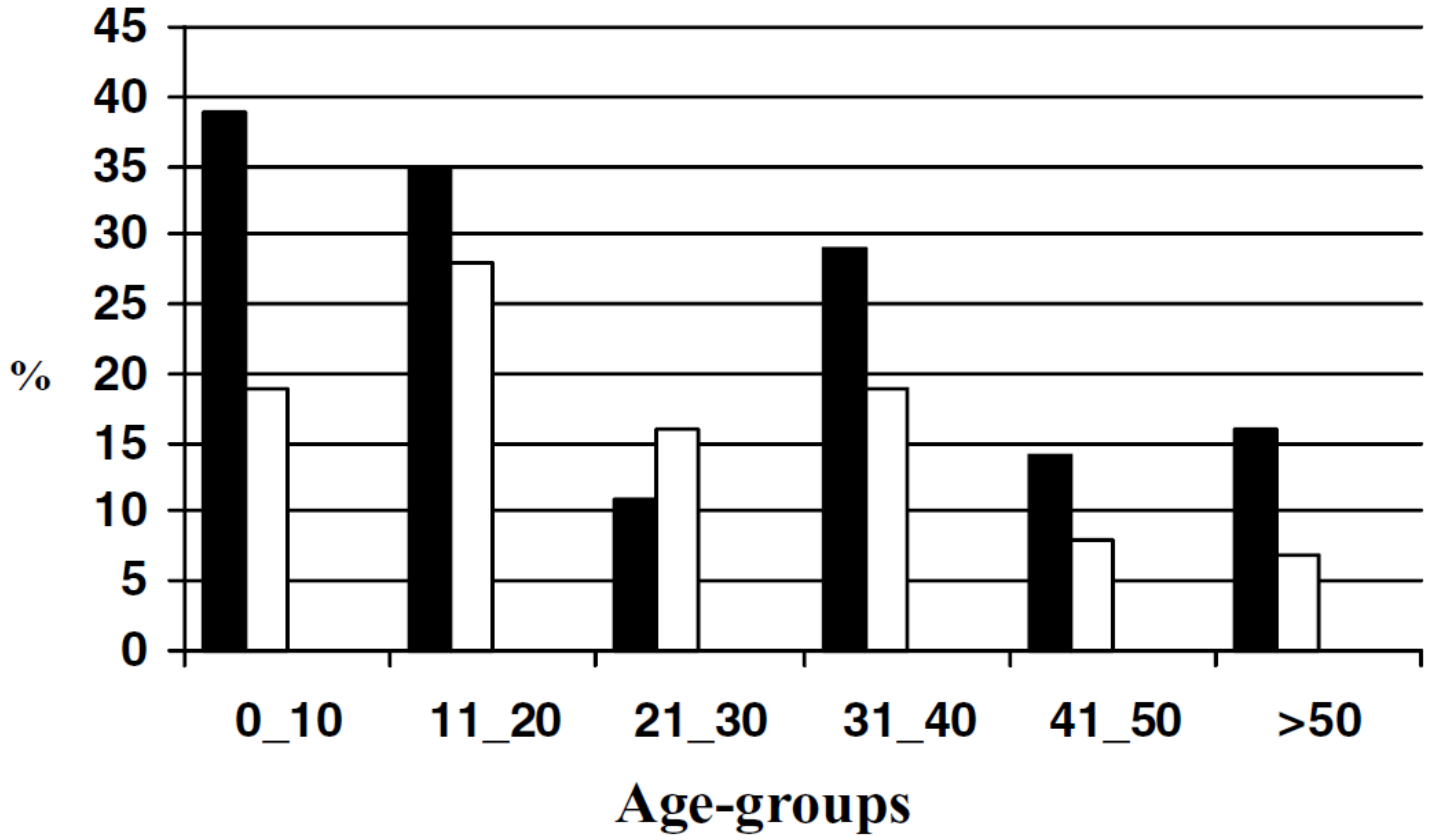
Changes in clinical symptoms?

Less autoimmune manifestations in elderly patients with CVID



Quinti I et al. J Clin Immunol 2007

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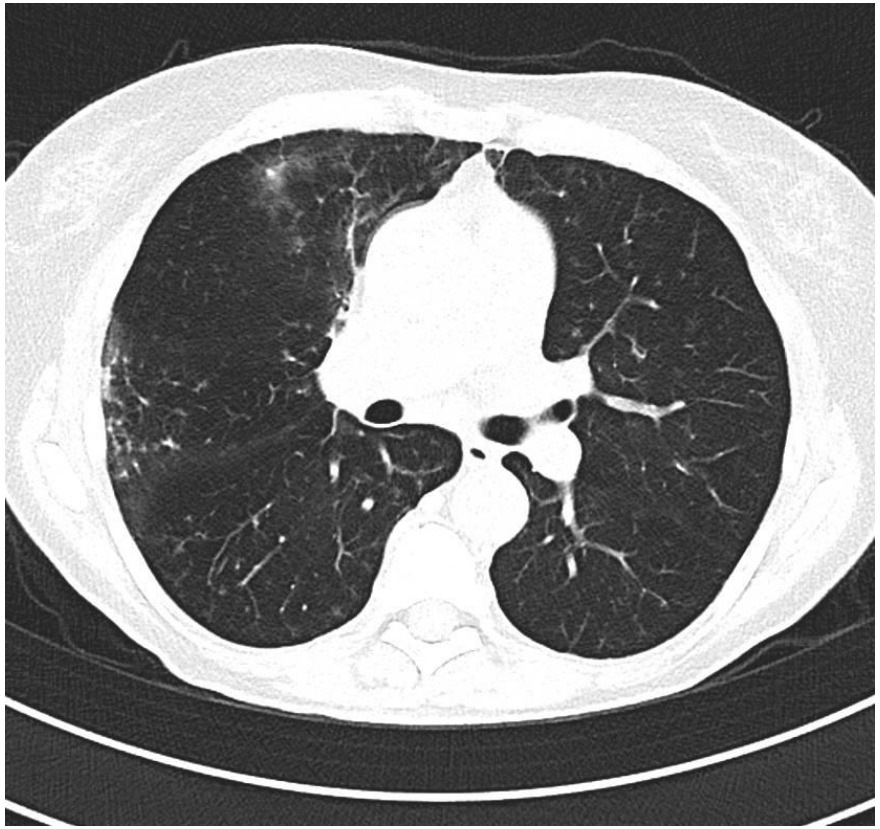
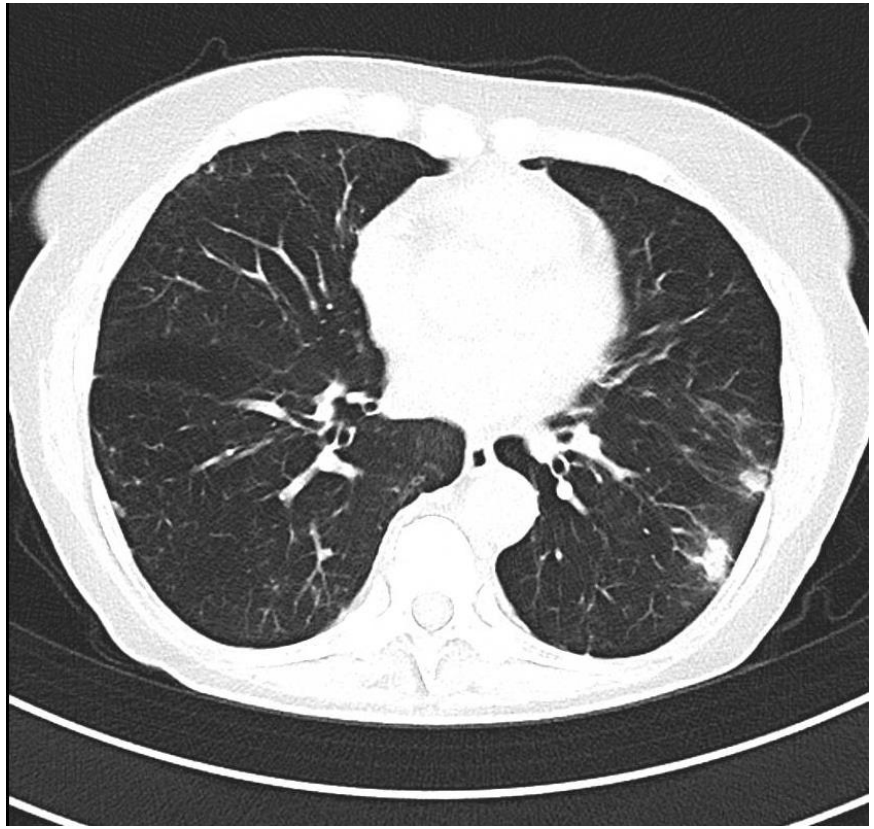
Back to our patient

CT-scan 2020 (age 79) : what to do?





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Changes in treatment?

IVIG in the elderly patient?

- Comorbidities including cardiovascular disease / renal disease
- The use of concomitant medication?
- Higher risk of adverse events?

High dose IVIG in elderly

Table 1. Demographic data and IVIg risk factors according to age

	<60 years old ($n = 92$)	≥60 years old ($n = 152$)	*P*-value
Men [*n* (%)]	51 (55)	102 (67)	0.07
Age [mean ± SD (range)]	47.1 ± 11.4 (16–59)	72.1 ± 7.6 (60–89)	**<0.001**
IVIg [mean ± SD (range)]			
Daily dose (g/kg)	30.3 ± 3.3 (10–40)	30.3 ± 2.0 (20–40)	0.95
Course dose (g/kg)	1.6 ± 0.38 (1–2.21)	1.8 ± 0.40 (0.91–2.09)	**0.01**
Sucrose-free [*n* (%)]	26 (28)	50 (33)	0.48
10% concentrated [*n* (%)]	24 (26)	47 (31)	0.42
Risk factors [*n* (%)]			
Number of patients with RF	44 (48)	4 (62)	**<0.001**
Number of RFs/patient [mean ± SD (range)]	0.7 ± 0.9 (0–3)	1.2 ± 0.9 (0–4)	**0.02**
Hypertension	18 (20)	50 (33)	**0.02**
Diabetes	9 (10)	15 (10)	0.98
Overweight	10 (11)	5 (3)	**0.02**
Renal insufficiency	5 (5)	6 (4)	0.59
Congestive heart failure	4 (4)	8 (5)	1
Stroke	0	7 (5)	**0.04**
Coronary artery disease	0	2 (11)	NA
Venous thrombosis	1 (1)	10 (7)	**0.05**
Walking aids	23 (25)	36 (24)	0.82
Monoclonal gammopathy	6 (7)	27 (18)	**0.01**

Lozeron P et al. Muscle Nerve 2015

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High dose IVIG in elderly

Dose of > 35 gram per day is associated with adverse reactions

Table 2. Relative risk of adverse reactions in old patients

	<60 years old ($n = 92$)	≥60 years old ($n = 152$)	Overall ($n = 244$)	Relative risk (95% confidence interval)
Adverse reactions [*n* (%)]	27 (33)	58 (38)	85 (35)	1.15 (0.86–2.6)
Immediate adverse reactions	24 (26)	56 (37)	80 (33)	1.22 (0.73–2.35)
Hypertension	18 (20)	50 (33)	68 (28)	**1.38** (1.41–5.29)
Headache	12 (13)	10 (7)	22 (9)	0.71 (0.19–1.14)
Nausea	1 (1)	2 (13)	3 (1)	1.07 (0.11–13.53)
Skin reaction	3 (3)	8 (5)	11 (5)	1.18 (0.43–6.38)
Fever	3 (3)	5 (3)	8 (5)	1 (0.24–4.33)
Delayed adverse reactions	5 (5)	18 (12)	23 (9)	1.29 (0.84–6.53)
Acute renal failure	2 (2)	3 (2)	5 (2)	0.96 (0.15–5.55)
Allergy	0	1 (1)	1 (0.5)	NA
Congestive heart failure	0	2 (1)	2 (1)	NA
Venous thrombosis*	1 (1)	5 (3)	6 (2)	1.35 (0.36–26.96)
Arterial thrombosis†	1 (1)	1 (1)	2 (1)	0.8 (0.04–9.71)
Hematologic reaction	0	2 (1)	1 (0.5)	NA
Meningitis	1 (1)	1 (1)	2 (1)	0.8 (0.04–9.71)
Other‡	5 (5)	9 (6)	14 (6)	1.03 (0.35–3.33)

Lozeron P et al. Muscle Nerve 2015

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Changes in treatment?

SCIG in elderly PID patients (n=47)

Self-infusion 83%

Safe

No serious AEs

No bruising/bleeding despite use of anti-platelet or anti-coagulant therapy in 45%

Table 1. Patient Demographics and Baseline Disease Characteristics

Parameter	Patients, n (%) N = 47
Age, years	
65–69	19 (40.4)
70–74	11 (23.4)
75–79	8 (17.0)
80–84	6 (12.8)
85–89	3 (6.4)

Stein MR et al. Postgraduate Medicine 2011.

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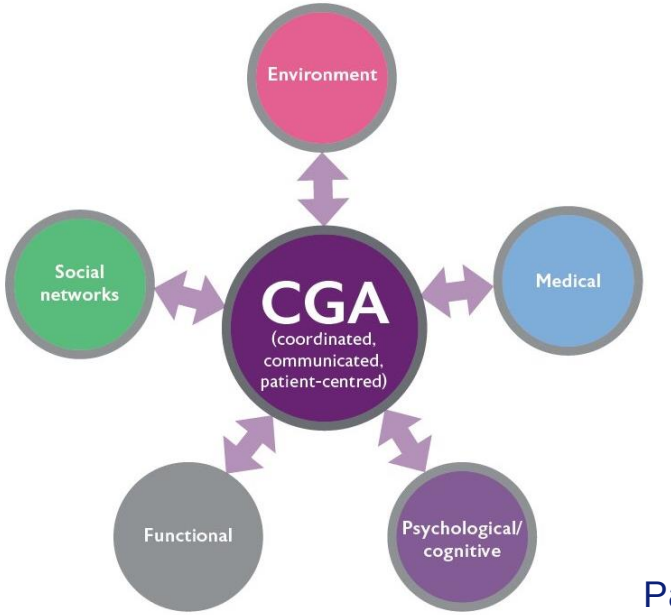
How to improve clinical care for the elderly?

Geriatric assessment in PID?

Comprehensive Geriatric Assessment (CGA)

“CGA is a multidimensional interdisciplinary assessment for evaluating the medical, psychological, physical functions and socioeconomic problems to detect unidentified and potentially reversible problems and develop a coordinated and integrated management plan for treatment and long-term care plan”



Parker SG et al. Age and Ageing 2018

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How to improve clinical care for the elderly?

New members of the multidisciplinary team in elderly PID?

- Geriatrician
- Dietician / nutritionist
- Rehabilitation specialist
- Oncologist
- ……..

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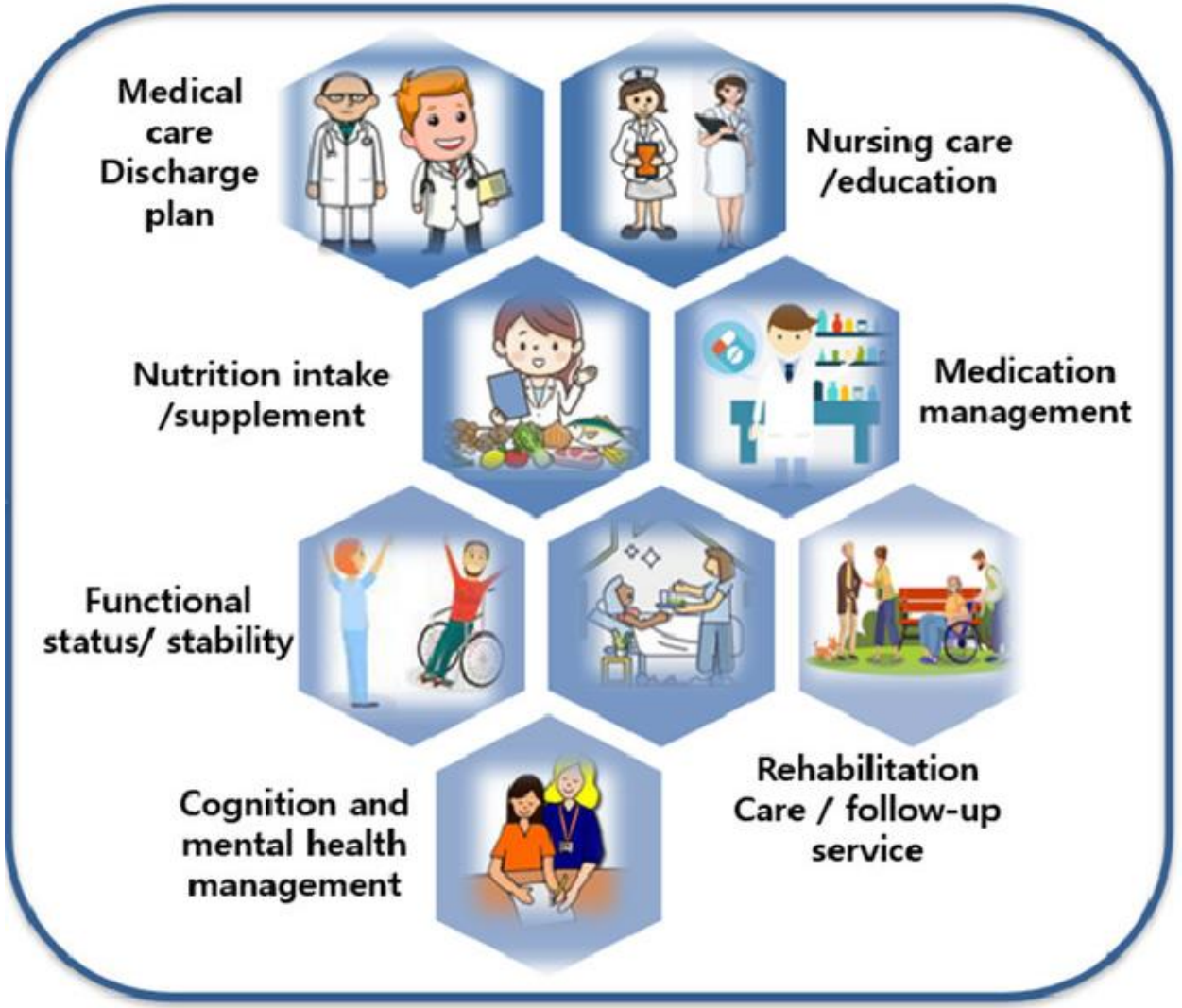
A new multidisciplinary team for elderly PID?



britishgeriatricssociety.wordpress.com; Choi JY et al. Archives of Gerontology and Geriatrics 2023

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