Update en stand van zaken MGUS polyneuropathie

Perry van Doormaal, neuroloog Tergooi MC, UMC Utrecht

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tergooimc

Wat is MGUS polyneuropathie?

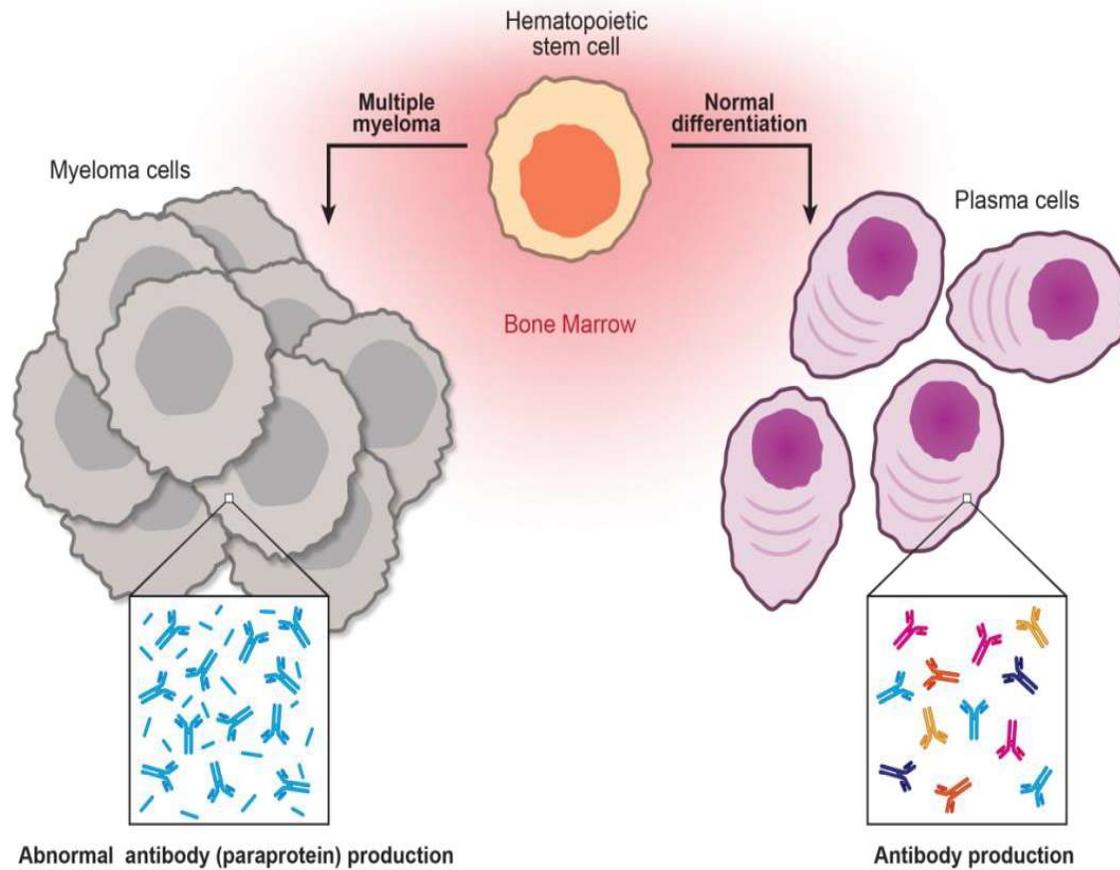MGUS **+** Polyneuropathie
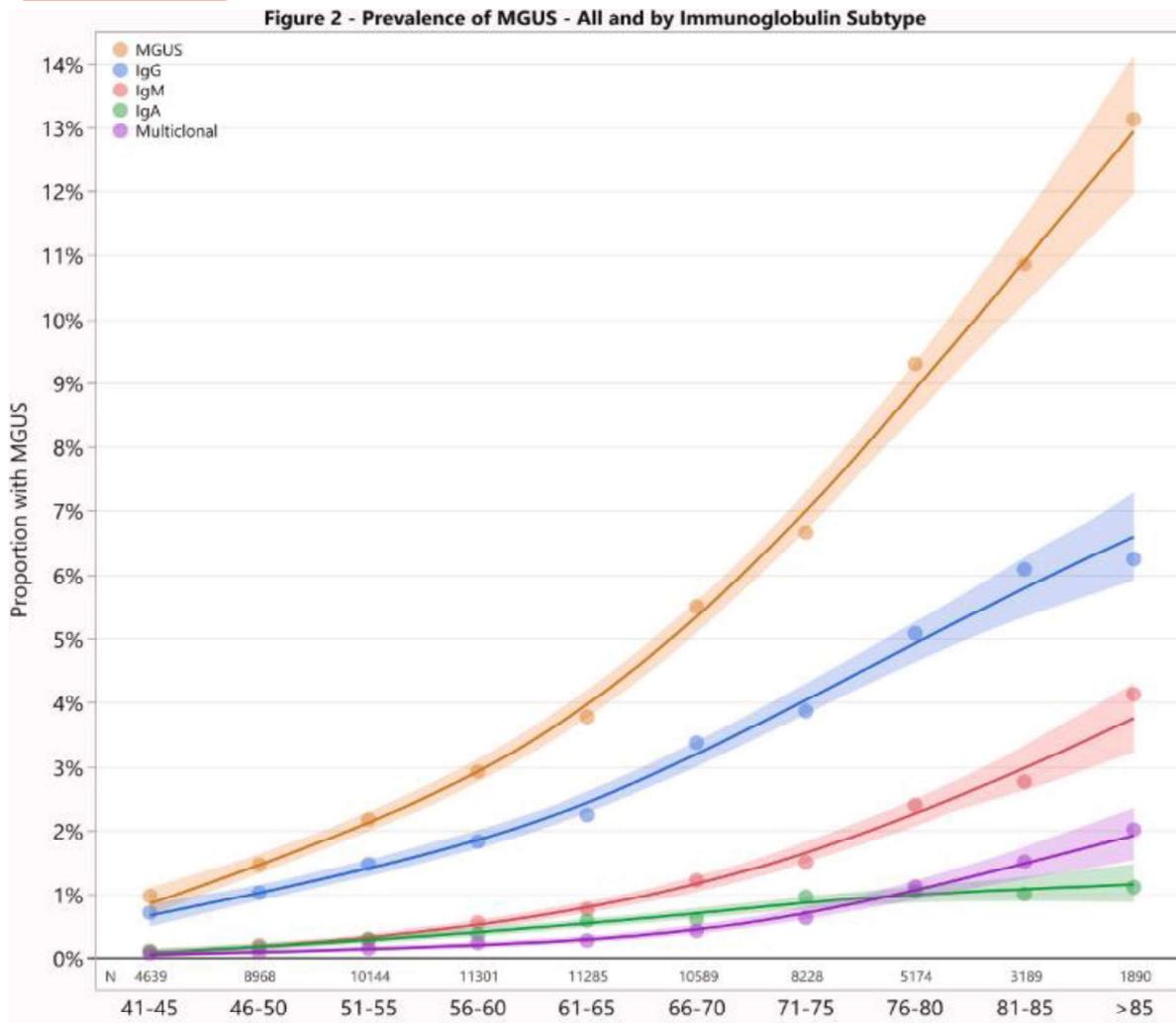
Wat is MGUS polyneuropathie?

| MGUS | + | Polyneuropathie |

Monoclonal gammopathy of unknown significance
M-proteine

M-proteine

IgM
IgG
IgA

MGUS is geen zeldzame aandoening

Figure 2 - Prevalence of MGUS - All and by Immunoglobulin Subtype

iStopMM

80,759
participated

Wat is MGUS polyneuropathie?

MGUS $+$ Polyneuropathie

Monoclonal gammopathy of unknown significance
M-proteine

IgG

IgM

IgA

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Polyneuropathie bij MGUS
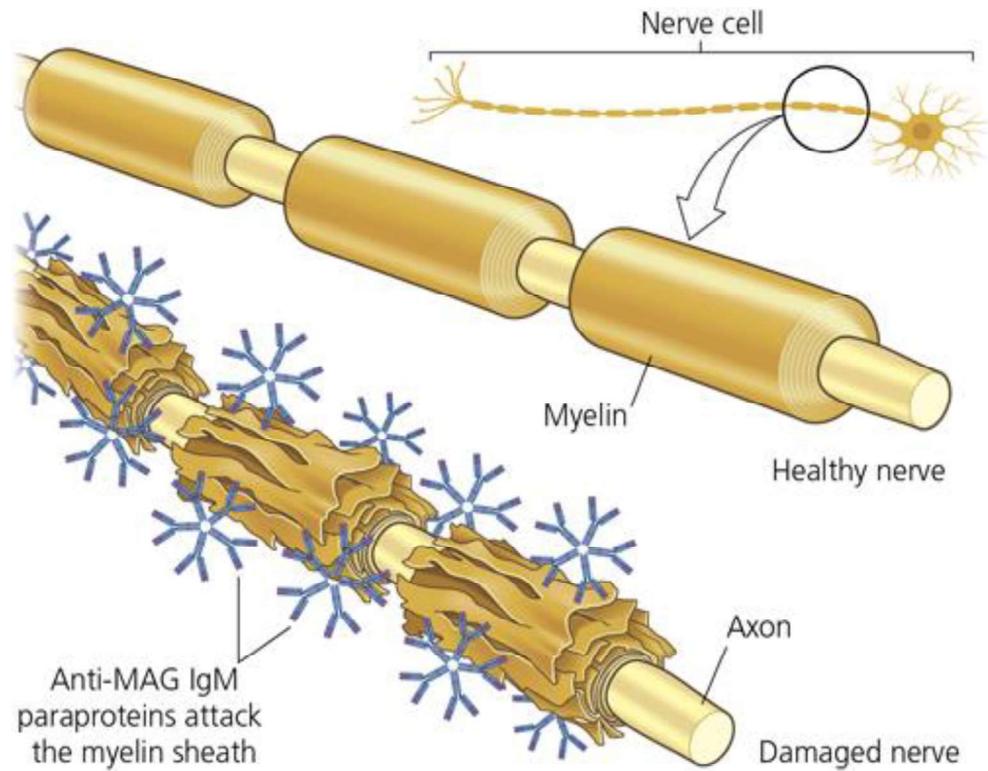
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Wat is MGUS polyneuropathie?

MGUS **+** Polyneuropathie

Monoclonal gammopathy of unknown significance
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IgM ⟶ Demyeliniserende polyneuropathie

IgA

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Wat is MGUS polyneuropathie?

MGUS **+** Polyneuropathie

Monoclonal gammopathy of **_unknown significance_**
M-proteine

IgG

IgM → Demyeliniserende polyneuropathie

IgA

IgM geassocieerde polyneuropathie

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Weinig voorkomende oorzaak van pnp

- Diabetic polyneuropathy — 32%
- Cryptogenic axonal polyneuropathy — 26%
- Toxic polyneuropathy[c] — 14%
- Immune-mediated polyneuropathy[e] — 9%
- Hereditary polyneuropathy — 5%
- Polyneuropathy with systemic disease[f] — 5%
- Metabolic polyneuropathy[g] — 4%
- Polyneuropathy with vitamin B_{12} deficiency[h] — 3%
- Idiopathic small fiber neuropathy — 2%

Behandeling

Hematopoietic stem cell

Multiple myeloma

Normal differentiation

Bone Marrow

Myeloma cells

Plasma cells

Abnormal antibody (paraprotein) production

Antibody production

Behandeling

Rituximab

Myeloma cells

Hematopoietic stem cell

Multiple myeloma

Normal differentiation

Bone Marrow

Plasma cells

Abnormal antibody (paraprotein) production

Antibody production

Behandeling

Rituximab

IVIG

Rituximab

Technique	Intervention	Design	Study Arms	Number of Patients	Outcome	Authors
Decreasing M-protein production by targeting B-cell	Rituximab (RTx)	Prospective, double-blind RCT. Follow-up 8 months	RTx vs. placebo	13 vs. 13 (all anti-MAG)	No significant improvement in primary outcome, but significant improvement in secondary outcome measures (e.g., 10 m walk test)	Dalakas et al., 2009. [155]
		Prospective, double-blind RCT. Follow-up 12 months	RTx vs. placebo	26 vs. 28 (all anti-MAG)	No significant improvement in primary outcome, but significant improvement in secondary outcome measures (e.g., INCAT disability scale)	Léger et al., 2013. [156]
		Pro- and retrospective, uncontrolled open-label case series. Follow-up 6–12 months	RTx	92 (all anti-MAG)	29 patients had a significant clinical improvement (ONLS and/or modified functional impairment scale score), 27 remained stable	Svahn et al., 2018. [101]
		Retrospective case series	RTx	25 IgM MGUS (23 anti-MAG), 8 WM (all anti-MAG)	18 of 33 patients clinically significant improvement (INCAT, INCAT sensory sum score, MRC sum score). MGUS statistically significant, WM not reached	Campagnolo et al., 2017. [157]

IVIG

Intervention	Design	Study Arms	Number of Patients	Outcome	Authors
Intravenous immunoglob-ulins (IVIG)	Randomized double-blind crossover trial. Follow-up 6 months (3 months for 1st treatment, 3 months for 2nd treatment)	IVIG vs. placebo	11 vs. 11 (9 anti-MAG)	2 patients had a short (<3 months) clinically significant improvement in neurological functions	Dalakas et al., 1996. [164]
	Randomized double-blind crossover trial. Follow-up 4 weeks	IVIG vs. placebo	11 vs. 11 (11 anti-MAG)	Significant clinical improvement after 4 weeks (INCAT score and 10 m walk test). Secondary outcomes significantly increased as well. No percentages of patients given. No data after follow-up	Comi et al., 2002. [165]

Overige behandelingen

Table 1

Technique	Intervention	Design	Study Arms	Number of Patients	Outcome	Authors
Scavenging M-protein	Plasma exchange (PE)	Prospective double-blind RCT. Follow-up 3 weeks	PE vs. sham exchange	19 (11 IgM) vs. 20 (10 IgM). No information on MAG status	Significant improvement in motor score in IgG and IgA paraprotein patients, but not for IgM paraprotein patients	Dyck et al., 1991. [150]
		Prospective, open-label RCT. Follow-up 12 months	PE + chlorambucil vs. chlorambucil	22 vs. 23 (16 & 17 antimyelin Abs, respectively)	No difference in clinical outcome	Oksenhendler et al., 1995. [151]
		Retrospective case series	PE	6 (all anti-MAG)	1 patient subjective improvement, 1 patient objective improvement but became unresponsive to PE later in disease course	Ellie et al., 1996. [91]
		Retrospective case series	PE / PE + chlorambucil	5 / 2 (all anti-MAG)	2/5 patients with PE alone improved, 2/2 patients with PE + chlorambucil improved on functional impairment scale. Effect duration not mentioned	Nobile-Orazio et al., 2000. [109]
		Retrospective case series	PE	20 (all anti-MAG)	8 patients had at least temporal neurological improvement on MRC sum scale and neurological impairment scale	Gorson et al., 2001. [152]
		Pro- and retrospective, uncontrolled open-label case series. Follow-up 6–12 months	PE	24 (all anti-MAG)	4 patients had a significant clinical improvement (ONLS and/or modified functional impairment scale score) after 6 months, 1 after 12 months	Svahn et al., 2018. [101]
		Retrospective case series	PE (in acute worsening)	4 (all anti-MAG)	4 patients improved on ONLS score and subjectively after 3 to 6 PEs	Baron et al., 2017. [153]
	Selective apheresis	Prospective case series. Follow-up 12 months	Selective apheresis	1 IgM (2 IgG). No information on MAG status.	Sensory and motor response	Siciliano et al., 1994. [154]

Table 2

Technique	Intervention	Design	Study Arms	Number of Patients	Outcome	Authors
Decreasing M-protein production by targeting B-cell	Rituximab (RTx)	Prospective, double-blind RCT. Follow-up 8 months	RTx vs. placebo	13 vs. 13 (all anti-MAG)	No significant improvement in primary outcome, but significant improvement in secondary outcome measures (e.g., 10 m walk test)	Dalakas et al., 2009. [155]
		Prospective, double-blind RCT. Follow-up 12 months	RTx vs. placebo	26 vs. 28 (all anti-MAG)	No significant improvement in primary outcome, but significant improvement in secondary outcome measures (e.g., INCAT disability scale)	Léger et al., 2013. [156]
		Pro- and retrospective, uncontrolled open-label case series. Follow-up 6–12 months	RTx	92 (all anti-MAG)	29 patients had a significant clinical improvement (ONLS and/or modified functional impairment scale score), 27 remained stable	Svahn et al., 2018. [101]
		Retrospective case series	RTx	25 IgM MGUS (23 anti-MAG), 8 WM (all anti-MAG)	18 of 33 patients clinically significant improvement (INCAT, INCAT sensory sum score, MRC sum score). MGUS statistically significant, WM not reached	Campagnolo et al., 2017. [157]
	Cyclophosphamide	Prospective, double-blind RCT, 2nd phase cross-over study. Follow-up 1st phase 6 months, 2nd phase 24 months	Cyclophosphamide + prednisone vs. placebo	16 vs. 19 (all anti-MAG)	No difference in primary outcome (Rivermead mobility index). Some secondary outcomes (e.g., MRC sum score, sensory sum score) improved significantly more than placebo after 24 months	Niermeijer et al. 2007. [158]
		Prospective, uncontrolled open-label case series. Follow-up mean 20 months (range 18–30)	Cyclophosphamide	9 (all anti-MAG)	7 patients significantly improved in muscle strength and modified ranking scale, 2 remained stable	Hamidou et al., 2005. [159]

Table 3

Technique	Intervention	Design	Study Arms	Number of Patients	Outcome	Authors
	Fludarabine	Prospective uncontrolled open-label case series. Follow-up mean 14.5 months (range 4–28)	Fludarabine	4 (2 anti-MAG)	4 patients significantly improved in motor and sensory neurological functioning and MRC sum score increase	Wilson et al., 1999. [160]
		Prospective uncontrolled open label case series. Follow-up 12 months	Fludarabine	16 (6 anti-MAG)	5 patients (all anti-MAG) significantly improved (1 point on median ranking scale), others were stable. Similar findings with Rivermead mobility index and MRC sum score	Niermeijer et al., 2006. [161]
	Cladribine	Case report	Cladribine + IVIG	1 (anti-MAG-positive)	Significant motor and sensory improvement (albeit after second IVIG trial)	Ghosh et al., 2002. [162]
	Chlorambucil	Retrospective case series	Chlorambucil	2 (both anti-MAG)	No significant difference in clinical outcome	Gorson et al., 2001. [152]
		Pro- and retrospective, uncontrolled open-label case series. Follow-up 6–12 months	Chlorambucil	33 (all anti-MAG)	1 patient had a clinically significant improvement (ONLS and/or modified functional impairment scale score), 8 remained stable	Svahn et al., 2018. [101]
	Melphalan	Prospective, uncontrolled open-label case series. Follow-up unknown	Melphalan + chlorambucil	1 (anti-peripheral nerve myelin Ab's)	No significant difference in clinical outcome	Ernerudh et al., 1992. [163]

Nieuwe behandelingen

- Hoe meten we vooruitgang
  - MGUS pnp specifieke uitkomstmaten
  - Voldoende deelnemers aan studies

- Bij wie moeten we de behandeling testen

- Waarom onderzoeken we niet ... of ...?

Technique	Treatment
Decreasing M-protein production by targeting B-cell	BTK inhibitors (e.g., ibrutinib, zanubrutinib, acalabrutinib)
	BCL2 inhibitors (Venetoclax)
	Anti-BCL2 monoclonal antibody (ulocuplumab)
	Next-generation anti-CD20 monoclonal antibodies (e.g., ofatumumab and obinutuzumab)
	Proteasome inhibitors (e.g., carfilzomib and ixazomib)
Decreasing damage by M-protein by immunosuppression or -modulation	Complement inhibitors (e.g., Cinryze, ARGX-117, compstatin family C3 inhibitors, and eculizumab)
Preventing the M-protein from binding/attacking target antigen	Autoantibody competitor decoys or antigen mimics (e.g., PPSGG)

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Waarom onderzoeken we niet ...

Home > Actueel > Nieuws >

Vanaf vandaag strengere regels voor nieuwe medische hulpmiddelen
Nieuwsbericht | 26-05-2021 | 08:00

De nieuwe Europese wetgeving voor medische hulpmiddelen is vanaf vandaag van toepassing. Dat betekent dat medische hulpmiddelen aan nog strengere eisen moeten voldoen voor ze op de Europese markt mogen komen. De Inspectie Gezondheidszorg en Jeugd ziet voor Nederland toe op deze wetgeving.

Een greep uit alle veranderingen:

- striktere controle bij hoog risico producten zoals implantaten voordat ze op de markt komen;
- nieuwe classificatieregels voor medische software;
- meer transparantie door verplichte registratie in een centrale Europese database, ook toegankelijk voor patiënten in EUDAMED;
- verbetering traceerbaarheid door een uniek identificatienummer (UDI) voor elk hulpmiddel;
- verplichting tot uitgebreidere monitoring op veiligheid en prestaties als een product op de markt is;
- duidelijke verantwoordelijkheid en aansprakelijkheidsstelling voor marktpartijen;
- striktere regels voor certificerende instanties (notified bodies) en het toezicht hierop.

Alle elementen van de MDR vallen onder ons toezicht. Zo zien we toe op de optimale veiligheid van de medische hulpmiddelen zelf en op het veilig gebruik van medische technologie door zorgverleners.
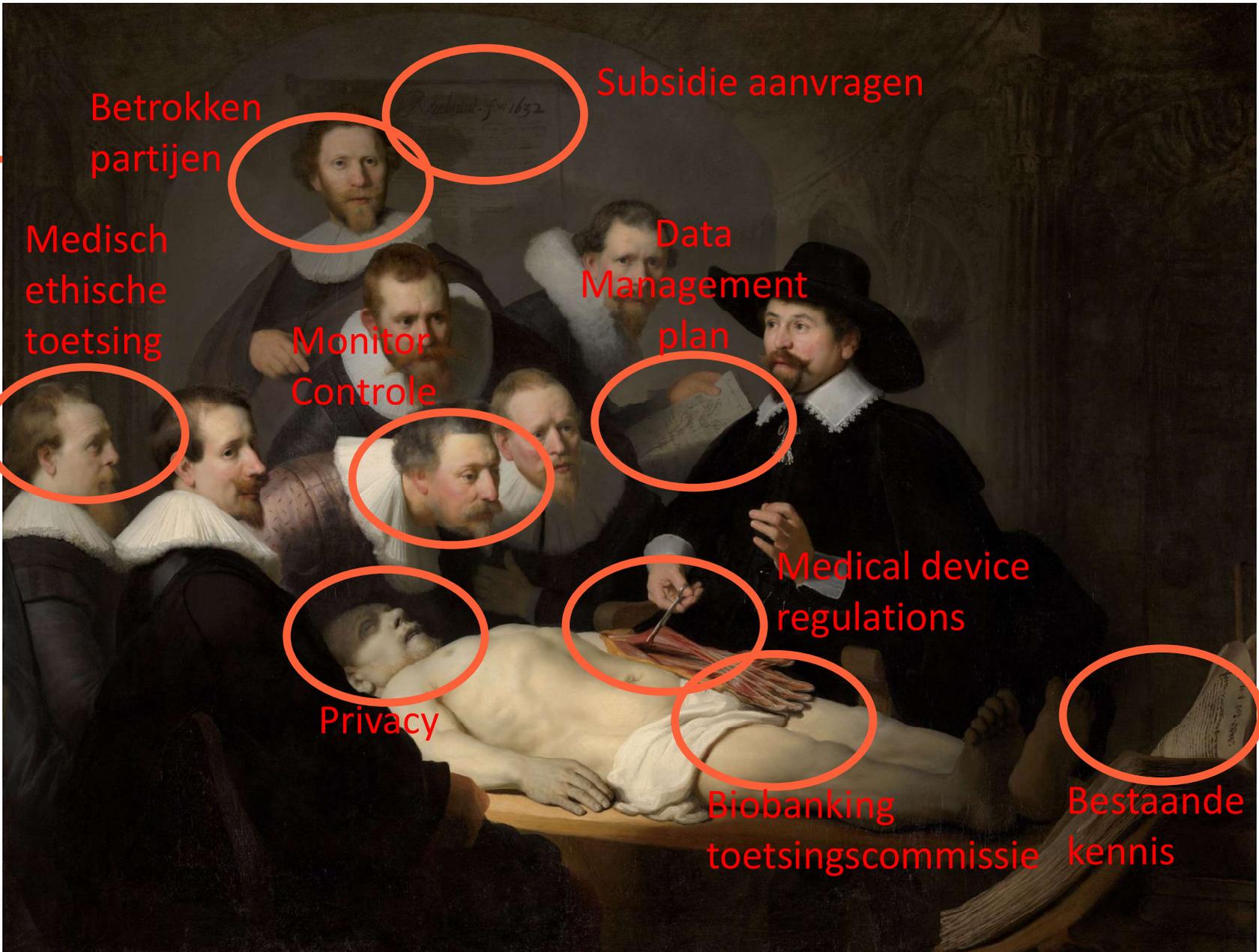
Handleiding Algemene Verordening Gegevensbescherming (AVG)
Rapport | 22-01-2018

Vanaf 25 mei 2018 geldt de Algemene Verordening Gegevensbescherming (AVG). Deze handleiding legt uit wat de AVG betekent voor partijen die persoongegevens verwerken. En aan welke regels de gegevensverwerking moet voldoen.

↗ Handleiding Algemene Verordening Gegevensbescherming (AVG) (PDF | 98 pagina's | 1,9 MB)

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Waarom onderzoeken we niet …

Elk onderzoek kost geld, tijd en middelen
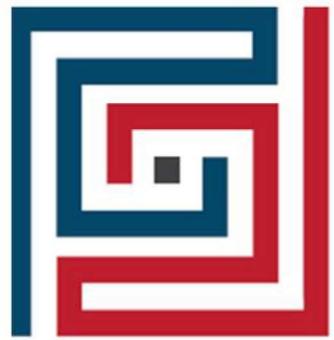
Beide zijn beperkt

Onderzoeken moeten daarom goed worden overwogen en optimaal worden opgezet

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Immunoglobulin **M**(IgM) ± **A**nti-myelin-associated-**g**lycoprotein (MAG) Peripheral **N**europathy Study

International/ Multi-center

Prospective

Observational cohort

Biobank

Web-Based Registry

IMAG±iNe study

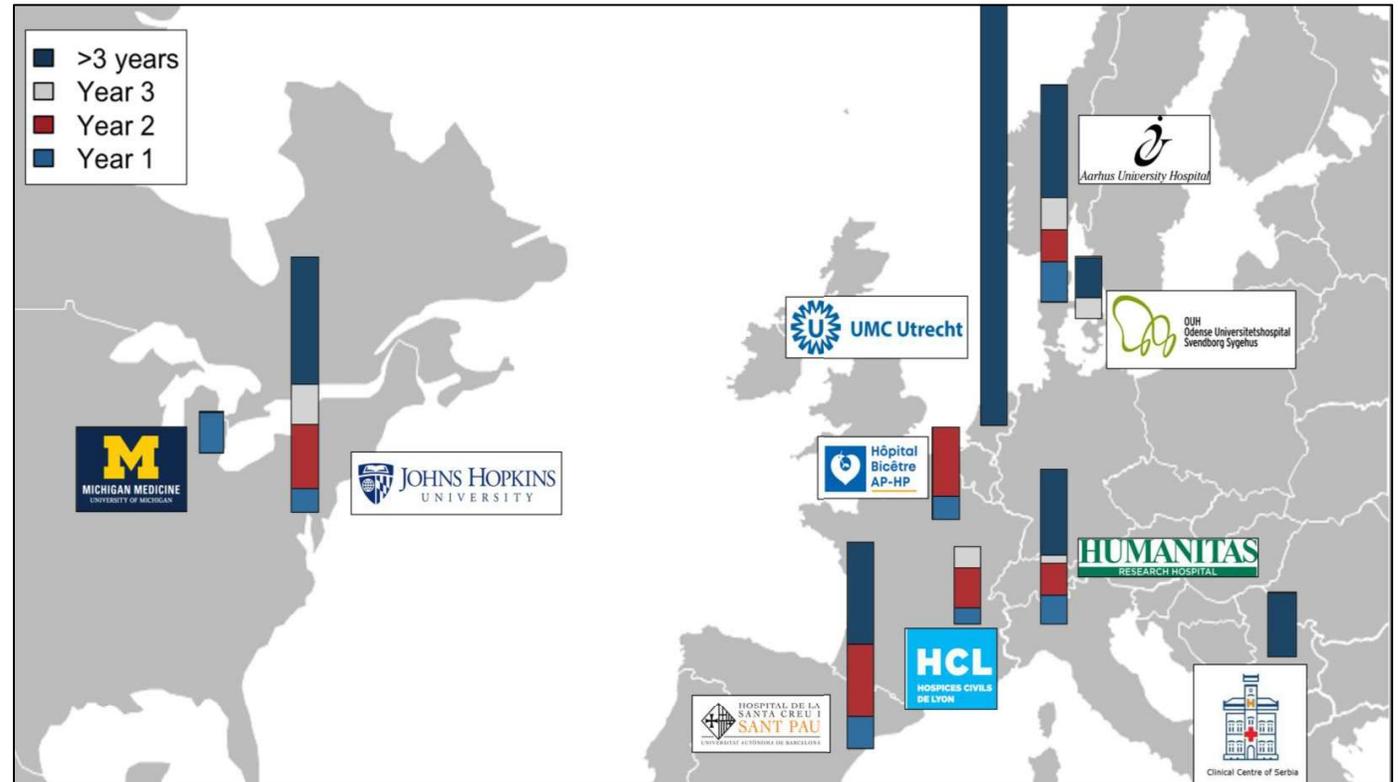|	
Register	Clinical characteristics Past/present treatment & their effects Lab Nerve conduction findings
Construct	**Activity & Participation** (IgM-PNP RODS) **Impairment** Ataxia rating scales - MGUSP
Describe & Identify	Subtypes Natural history Lab dynamics (biomarkers) Treatment regimes & efficacy

2023

- 252 patients in total
- 32 new patients in 2023 (+15%)
- Started follow-up after year 3

Stap terug om daarmee vooruit te komen