



Sint Maartenskliniek

## Post EULAR 2022



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Sint Maartenskliniek, Nijmegen  
Radboudumc, Nijmegen

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## Na 2 jaar, veranderde wereld



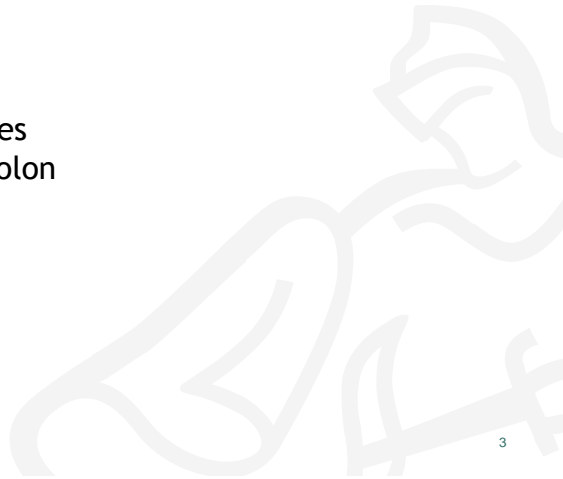
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## Inhoud

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- lets te vieren
- Veiligheid JAK
- Conditioneren
- Covid en vaccinaties
- Lage dosis prednisolon

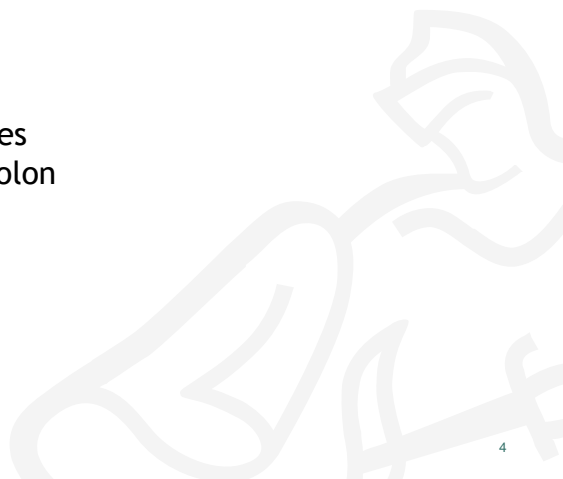


## Inhoud

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- **lets te vieren**
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## Ook iets te vieren..



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## Doel en methode



Verbeteren therapietrouw via impliciete cues

Entertaining  
4 soorten puzzles  
150 puzzles total

Engaging  
- 'Medi & Seintje'  
- Wereldrecord

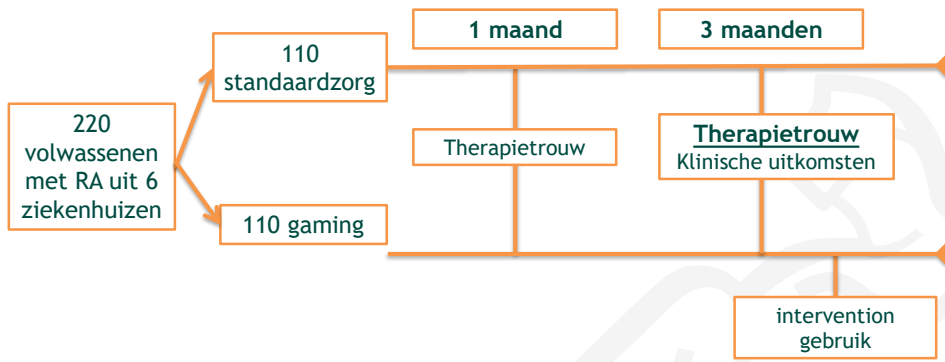


\* Published at <https://games.jmir.org/2022/1/e31570>

## Clinical trial\*



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\* Trial registration at <https://www.trialregister.nl/trial/7217>

## Resultaten: hoe lang werd er gespeeld?



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- Patiënten:
  - 2.026 uitgenodigd → 229 gestart → 186 studie afgerond
  - Gem. leeftijd: 61 jaren ± 12
  - 162 (73%) vrouwen
  - Mediane ziekteduur: 10 jaar (IQR: 4 - 16 jaar)

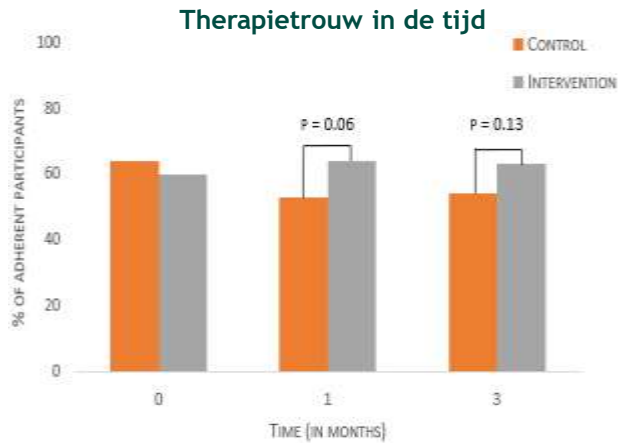
- Gebruik interventie

	1 maanden (N=86)	3 maanden (N=78)
Totale speltijd (uren)	6.2 [2.3 - 11.9]	9.7 [3.3 - 24.3]
Aantal sessies	16 [6 - 36]	36 [11 - 78]
Aantal triggers afgemaakt	20 [7 - 50]	46 [13 - 115]
Actieve timespanne [maximum 90 days]		87 [40 - 90]

## Resultaten: therapietrouw



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## Inhoud



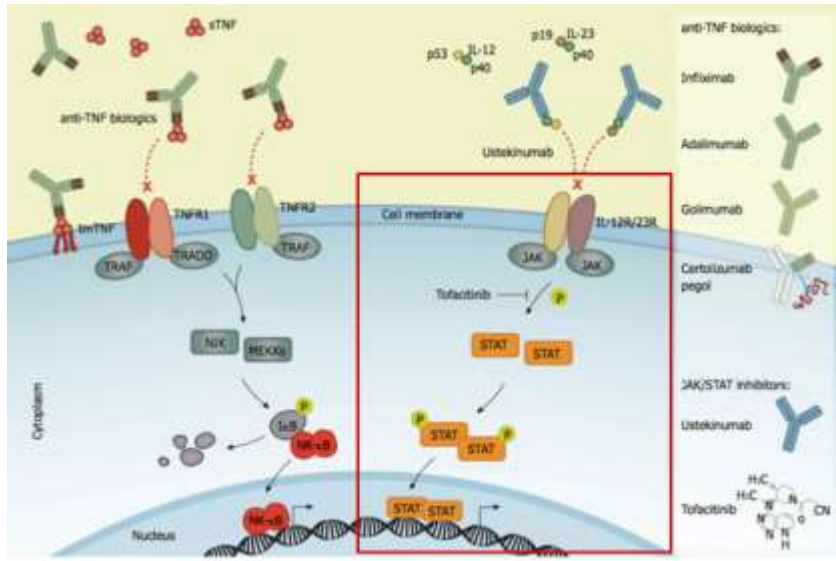
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- Iets te vieren
- **Veiligheid JAK**
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# JAK-inhibitors



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Pederson 2014

# JAK-remmers



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	belangrijke target	JAK remmer + MTX	afékinumab + MTX	
		ACRSO score na 24-26 weken	ACRSO score na 24-26 weken	
baricitinib 1 x daags 4 mg	JAK1, JAK2	51%	43%	Taylor 2017 [2]
filgotinib 1 x daags 200 mg	JAK1	54%	53%	Combe 2019 [3]
tofacitinib 2 x daags 5 mg	JAK3, JAK1	48%	44%	Fleischman 2017 [4]
upadacitinib 1 x daags 15 mg	JAK1	42%	54%	Fleischman 2017 [5]

Van den Bemt 2020

# Veiligheidssignalen



**Xeljanz**  
Indicated for:  
Lung Disease  
Pancreatic Cancer

**FDA WARNING** AUG 22, 2017

**EUROPEAN MEDICINES AGENCY**  
EMA starts safety review of Janus kinase inhibitors for inflammatory disorders

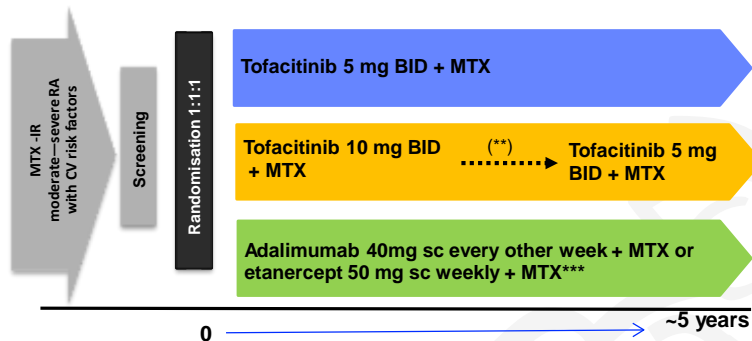
News 13/03/2022

EMA's safety committee, PRAC, has started a review of the safety of Janus kinase (JAK) inhibitors used to treat several chronic inflammatory disorders (rheumatoid arthritis, psoriatic arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, Crohn's disease and ulcerative colitis).

The review was prompted by the final results from a clinical trial (study A2231133) [1] of the JAK inhibitor Xeljanz (Tofacitinib). The results showed that patients taking Xeljanz for rheumatoid arthritis and who were at risk of heart disease were more likely to experience a major cardiovascular problem (such as heart attack, stroke, coronary artery disease and total atherosclerotic burden) than those treated

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# ORAL SURVEILLANCE



Study populatië  
RA ≥50 jaar  
≥1 CV risico factor  
MTX-IR  
Randomized, open-label  
~4000 pts, ~5 years\*

Ytterberg 2022

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## ORAL SURVEILANCE: uitkomstenmaten



- Major Adverse Cardiovascular Events (MACE)
- Maligniteiten (m.u.v. non-melanoma huidkanker)

### Definitie of MACE:

- Cardiovasculair overlijden
- Niet-fatale myocard infarct
- Niet-fatale stroke

Ytterberg 2022

## Cardiovasculair risico (samengevat)

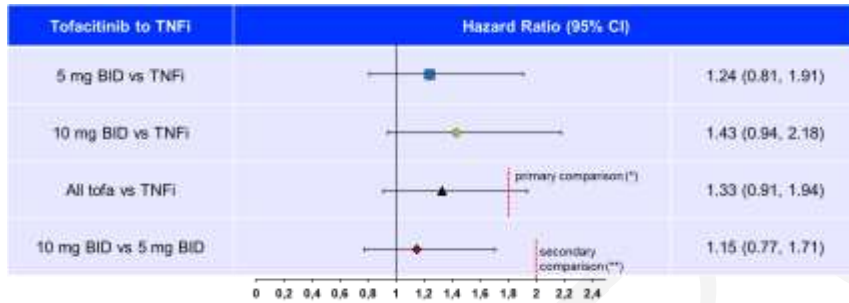


- Roken
- Hypertensie
- HDL <40 mg/dL
- Diabetes mellitus
- Voorgeschiedenis hart- vaatziektes
- Revascularisatie procedure
- Premature hartziekten in de eerste graads familie

Ytterberg 2022



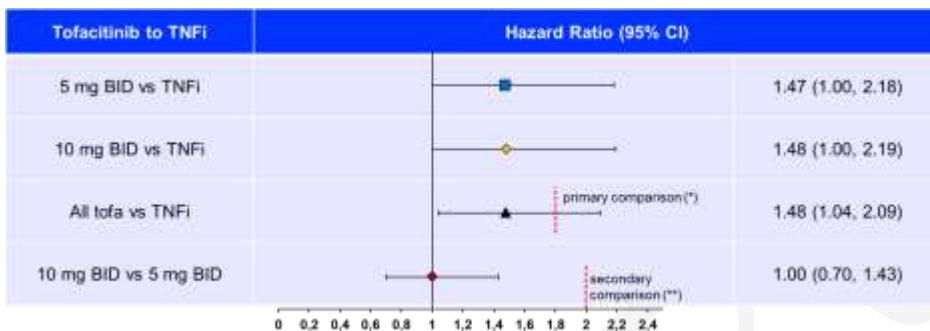
## ORAL SURVEILANCE: primaire uitkomst MACE



NNH=113

Ytterberg 2022

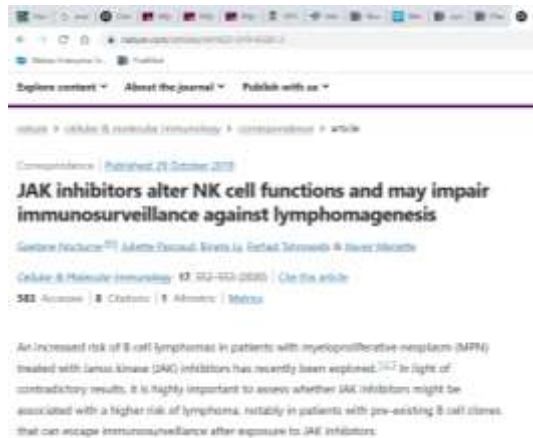
## ORAL SURVEILANCE: primaire uitkomst maligniteiten



NNH=55

Ytterberg 2022

## Waarom meer kanker ? Rol JAK-3?



## Baricitinib: op basis van RCTS



**Table 3.** Incidence of MACE, ATE, CHF, and DVT/PE by data analysis set\*

Event	Placebo-controlled (to week 24)			2 mg-4 mg-extended		
	Placebo (n = 1,073)	2 mg bar (n = 479)	4 mg bar (n = 997)	2 mg bar (n = 479)	4 mg bar (n = 479)	All-bar-BA (n = 3,492)
MACE†	2 (0.5%)	0#	3 (0.3%)	1 (0.2)#	2 (0.4)#	38 (0.5)
MI	1 (0.3%)	0#	1 (0.3%)	1 (0.2)#	1 (0.2)#	17 (0.2)
CV-related death	1 (0.3%)	0#	2 (0.5%)	0#	1 (0.2)#	11 (0.2)
Stroke	1 (0.3%)	0#	1 (0.3%)	0#	1 (0.2)#	15 (0.2)



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## EULAR recommendations

With respect to safety, beyond what was known to the task force and further corroborated in the course of the cut safety SLR such as an increased risk of herpes zoster infectio a new safety issue, namely VTEs including pulmonary embol has emerged for both baricitinib (4 mg daily)<sup>88</sup> and tofacit (at both 5 mg and especially 10 mg twice daily particular patients with risks of thromboembolic events and higher ag These latter data on tofacitinib are derived from an interim : ysis of study A3921133 (NCT02092467), an ongoing study compares tofacitinib at 5 and 10 mg twice daily with TNF i bition regarding major cardiovascular events and malignan patients with RA and at least one cardiovascular risk fac Thromboembolic events have also been observed with upa itinib.<sup>91,92</sup> VTEs are seen especially in patients with a high for these events (see safety SLR), such as those with a prev history of thromboembolic events, those with high body i index, those with hormone replacement therapy and hi age.<sup>90,93</sup> Therefore, JAKi should be used with caution in pati with high risk of TE events. Moreover, currently informu regarding this risk is not yet final and further accruing, at is not understood which mechanisms may drive this risk; should become a major target of research.

Smolem 2020



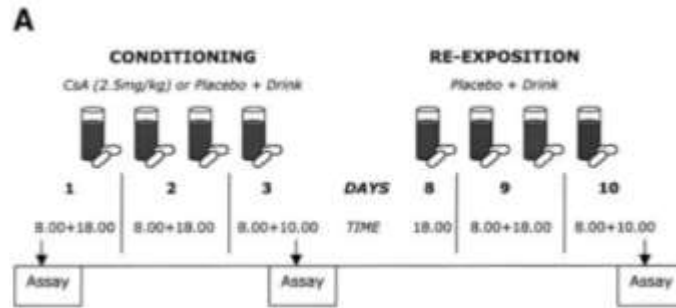
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## Twee thema's en opvallende zaken

- lets te vieren
- Veiligheid JAK
- **Conditioneren**
- Covid en vaccinaties
- Lage dosis prednisolon



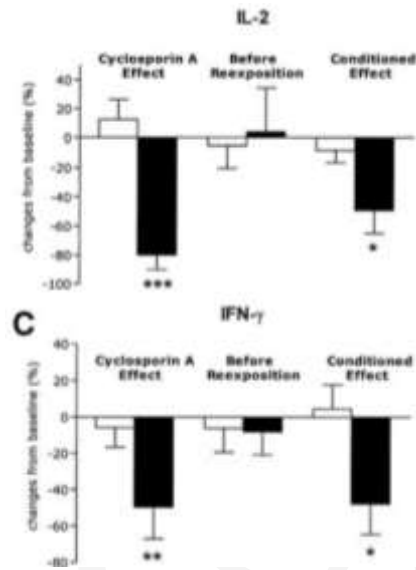
# Conditioneren: placebo



Goebbel 2002

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## Effect op interleukine-2 en interferron gamma



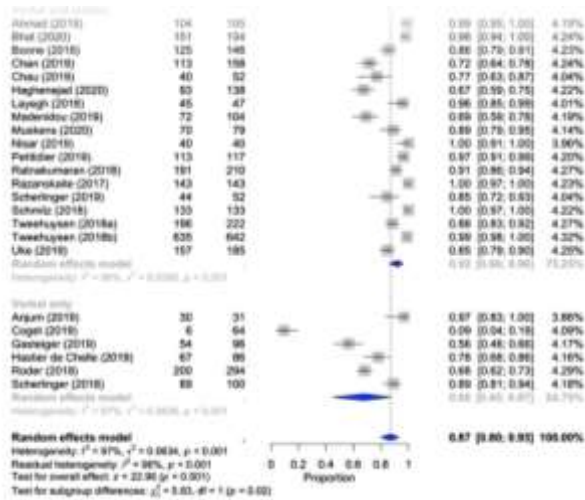
Goebbel 2002

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## Nocebo bij switchen



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87% wil switchen

Mondelinge- en schriftelijke informatie

Of schriftelijke informatie met weinig zorgen

Gasteiger 2022

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## Inhoud



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- Iets te vieren
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## Krijgen van COVID?



Ik heb reumatoïde artritis, heb ik meer kans op het krijgen van COVID-19?



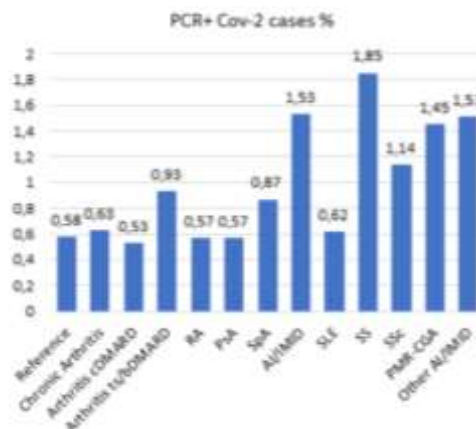
	Algemene populatie	Patiënten met ontstekingsreuma
Totaal	1.814.000	10.771
Besmet	5120 (0,28%)	30 (0,25%)

Aries 2020

## Krijgen van COVID?



Ik heb reumatoïde artritis, heb ik meer kans op het krijgen van COVID-19?



Pablos 2020

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## Krijgen van COVID?



Ik heb reumatoïde artritis,  
heb ik meer kans op het krijgen van COVID-19?

Table 1 EULAR recommendations for the management of rheumatic and musculoskeletal diseases in the context of SARS-CoV-2: the November 2021 update

Deciphering principles	Link, main ID#	% 2021
1. In general patients with RMDs do not face higher risk of contracting SARS-CoV-2 than individuals without RMDs, and do not have a worse prognosis when they contract it.	RIS (1,2)	101

Nee

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## Krijgen van COVID?

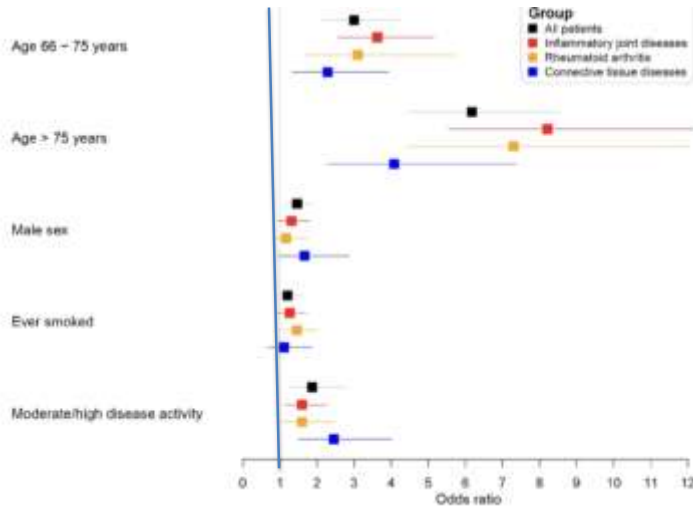


Welke factoren zorgen wel  
voor een grotere kans op COVID 19?

- Ziekteactiviteit
- NSAIDs
- Corticosteroïden
- Hydroxychloroquine
- Methotrexaat
- Anti-TNF
- Rituximab

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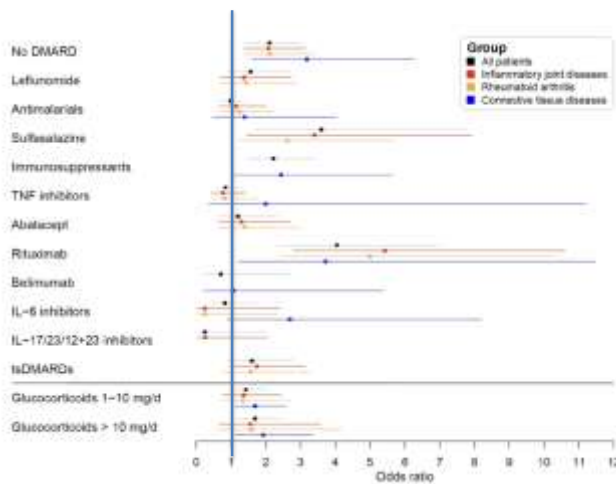
## Wanneer heb je meer kans op COVID?



Strangveld 2020

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## Wanneer heb je meer kans op COVID?



Strangveld 2020

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## Krijgen van COVID?



Welke factoren zorgen wel voor een grotere kans op COVID 19?

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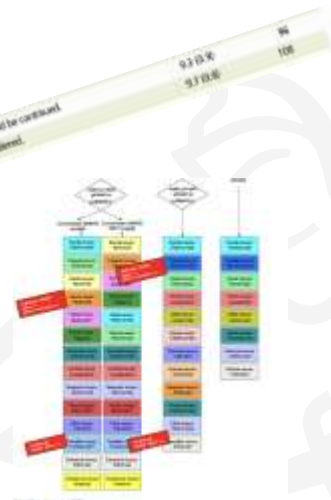
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## Krijgen van COVID?



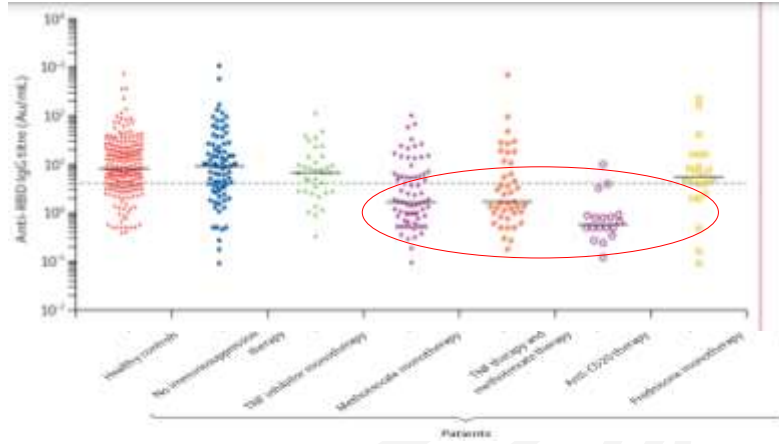
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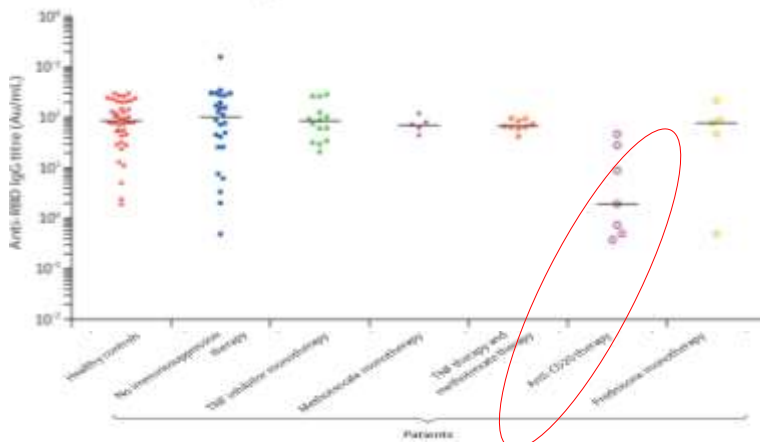
# Eerste vaccin



Boekel 2021

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# Tweede vaccin



Boekel 2021

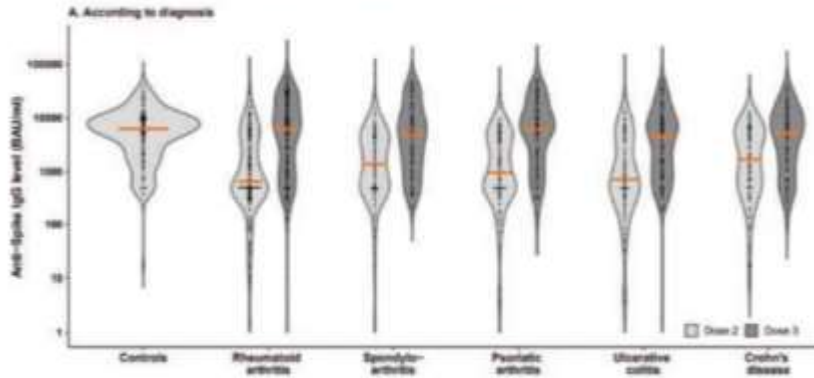
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## Derde vaccinatie



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Figure. Serological response of three-dose SARS-CoV-2 vaccination in patients with immune mediated inflammatory diseases on immunosuppressive therapy as compared to two dose vaccination in healthy controls.



Jyssum OP192 EULAR 2022

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## Rituximab



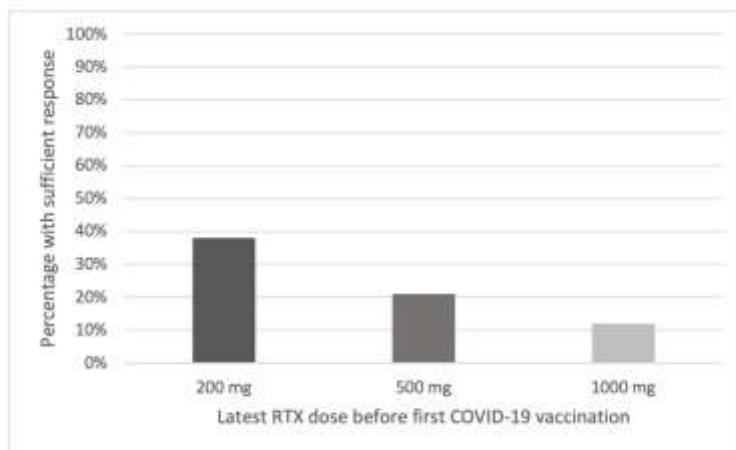
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**Conclusion** More than half of fully vaccinated individuals with breakthrough infections requiring hospitalisation were on BCDT or mycophenolate. Further risk mitigation strategies are likely needed to protect this selected high-risk population

Lieuw 2022

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## Wanneer heb je meer kans op COVID?



Vd Toegt 2022

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## Bescherming van het COVID vaccin?



Als je reumageneesmiddelen gebruikt blijft het COVID vaccin altijd even goed werken?

**Nee, rituximab niet**  
**Andere middelen wel**  
 (meer data nodig abatacept en JAK-remmers)

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## Inhoud

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- Iets te vieren
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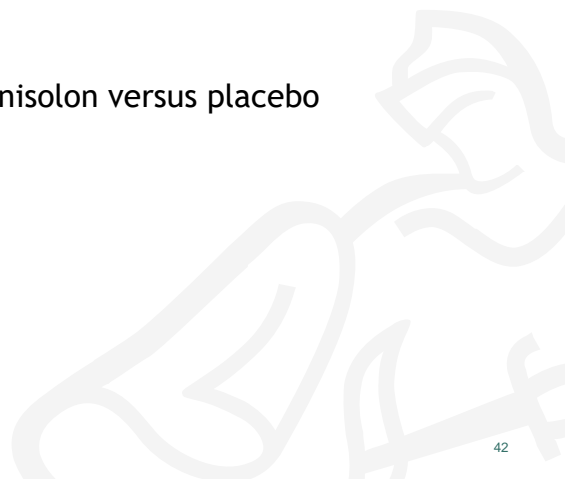


## GLORIA trial

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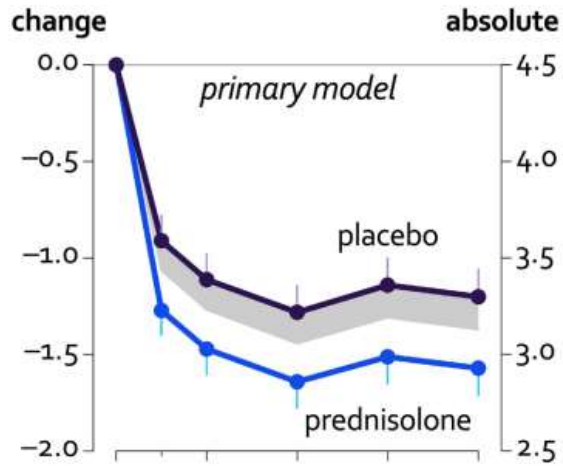
- Actieve RA
- Leeftijd 65 plus
- 5 mg per dag prednisolon versus placebo





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# GLORIA trial: effect



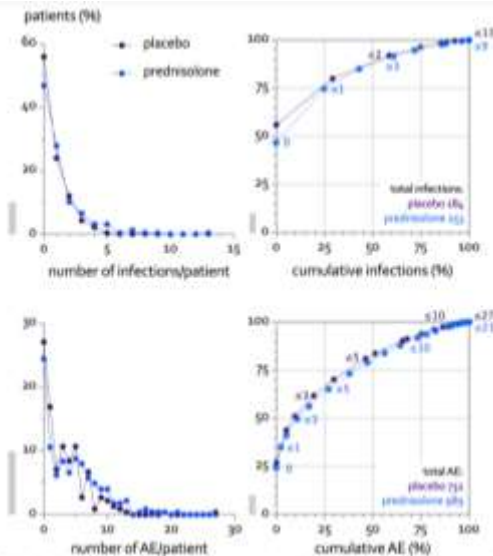
Boers 2022

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# GLORIA trial: bijwerkingen



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Boers 2022

fig 3. Patients with multiple adverse events (AE) have a major impact on the total number of events in both treatment groups, selected one

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## Inhoud

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- Iets te vieren
- Veiligheid JAK
- Conditionering
- Covid en preventies
- Lage dosis prednisolon

Dank voor uw aandacht!  
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