



Τι νεότερο σε ΡΑ  
Υπάρχει δυνατότητα να εμποδίσουμε την εξέλιξη  
της νόσου παρεμβαίνοντας πρώιμα?



ΕΠΕΜΥ Σεπτ 2023, Ηράκλειο

Δαούσης Δημήτρης  
Αναπλ. καθηγητής Παθολογίας/Ρευματολογίας  
Ιατρική Σχολή Πανεπιστημίου Πατρών

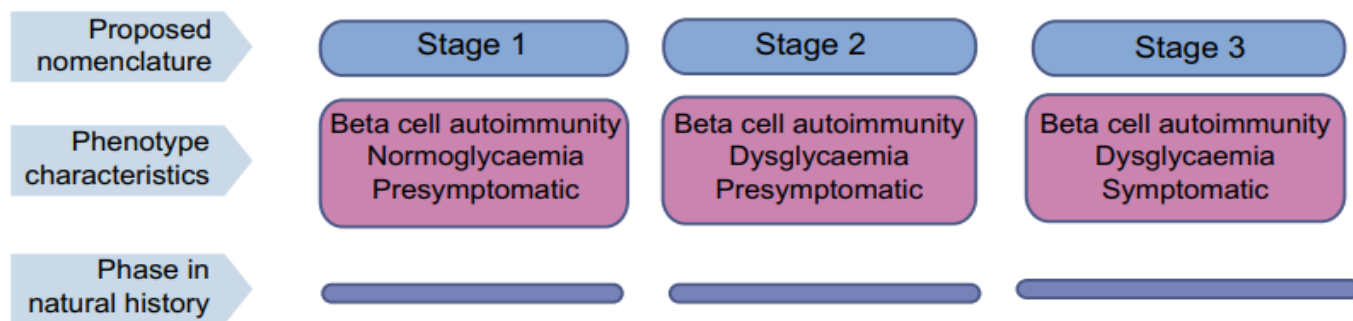
# Σύγκριση συμφερόντων

- Καμία για την παρούσα παρουσίαση

# Το σκεπτικό....

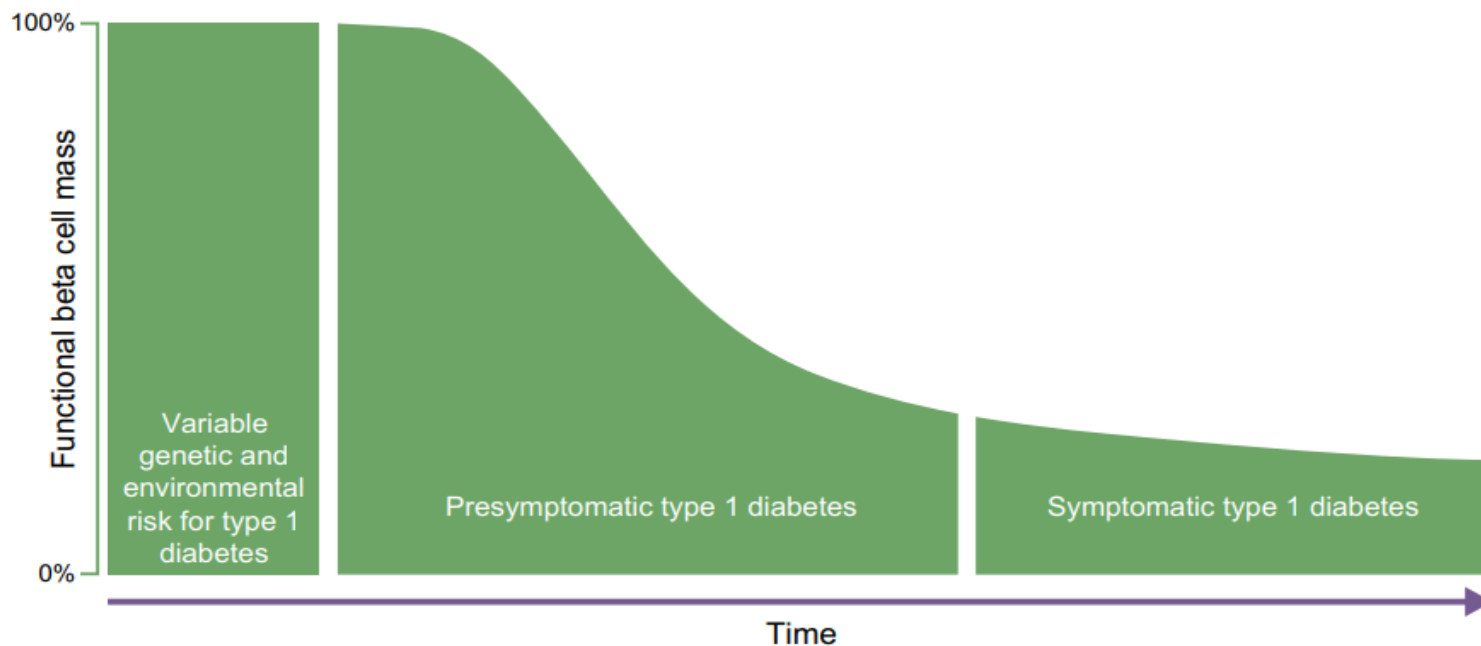


# Το παράδειγμα του Διαβήτη τύπου Ι....



Confirmed targets of autoantibodies in type 1 diabetes

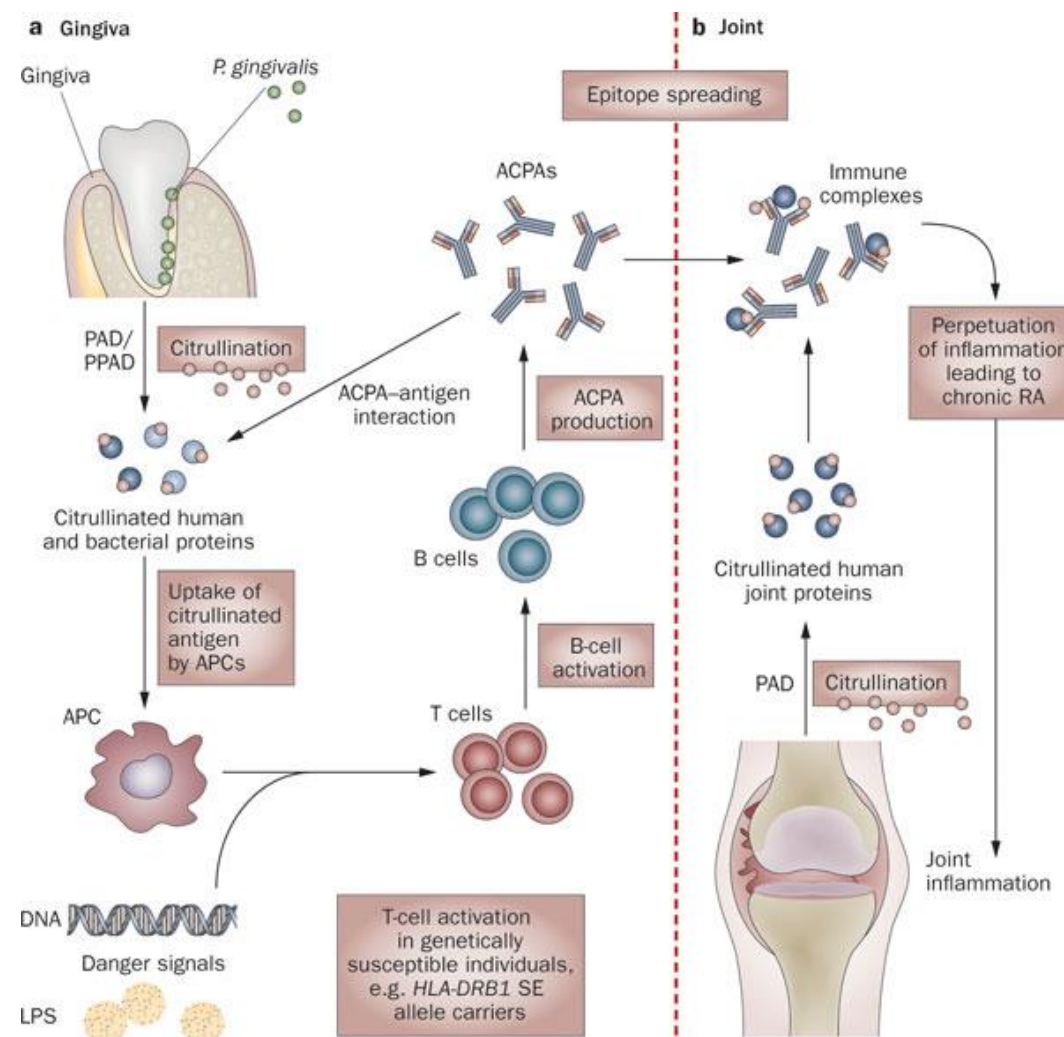
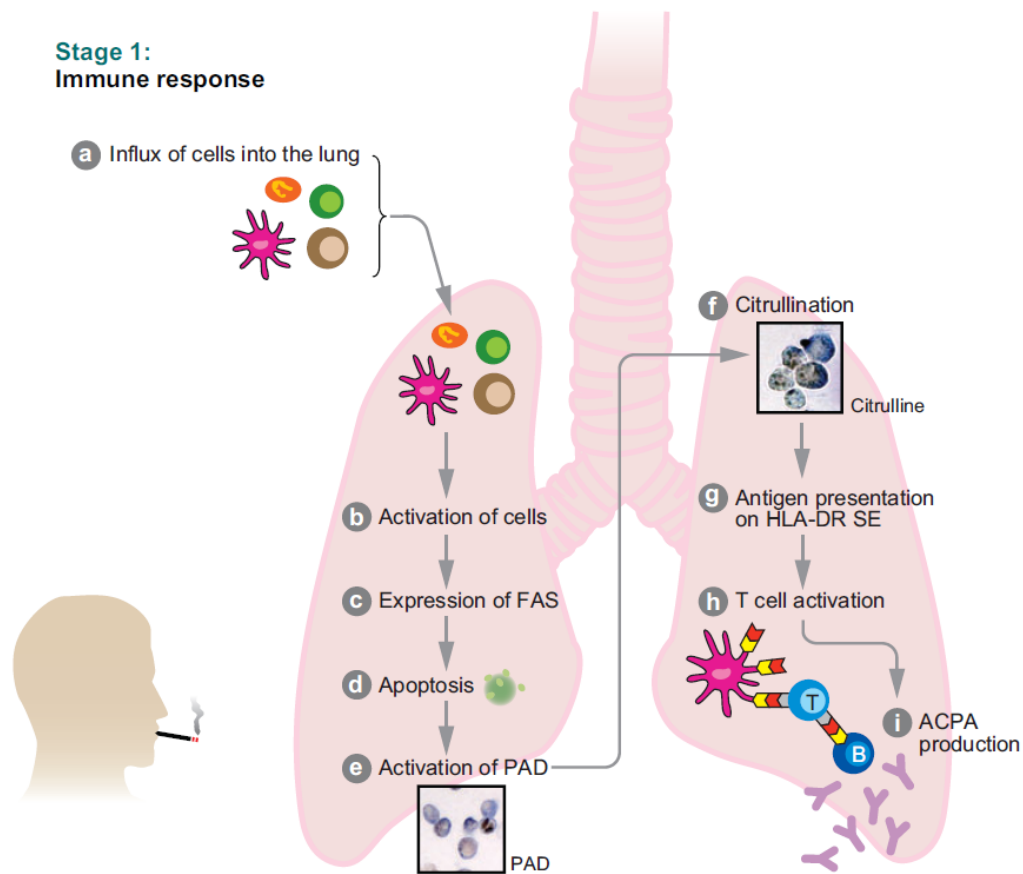
Insulin
Glutamic acid decarboxylase
Insulinoma associated antigens 2 (alpha and beta)
ZnT8 (zinc transporter)



- Τα αυτοαντισωματα προυπάρχουν των κλινικών εκδηλώσεων

# Η παθογένεια της RA ίσως ξεκινά από τους πνεύμονες ή τα ούλα!!!

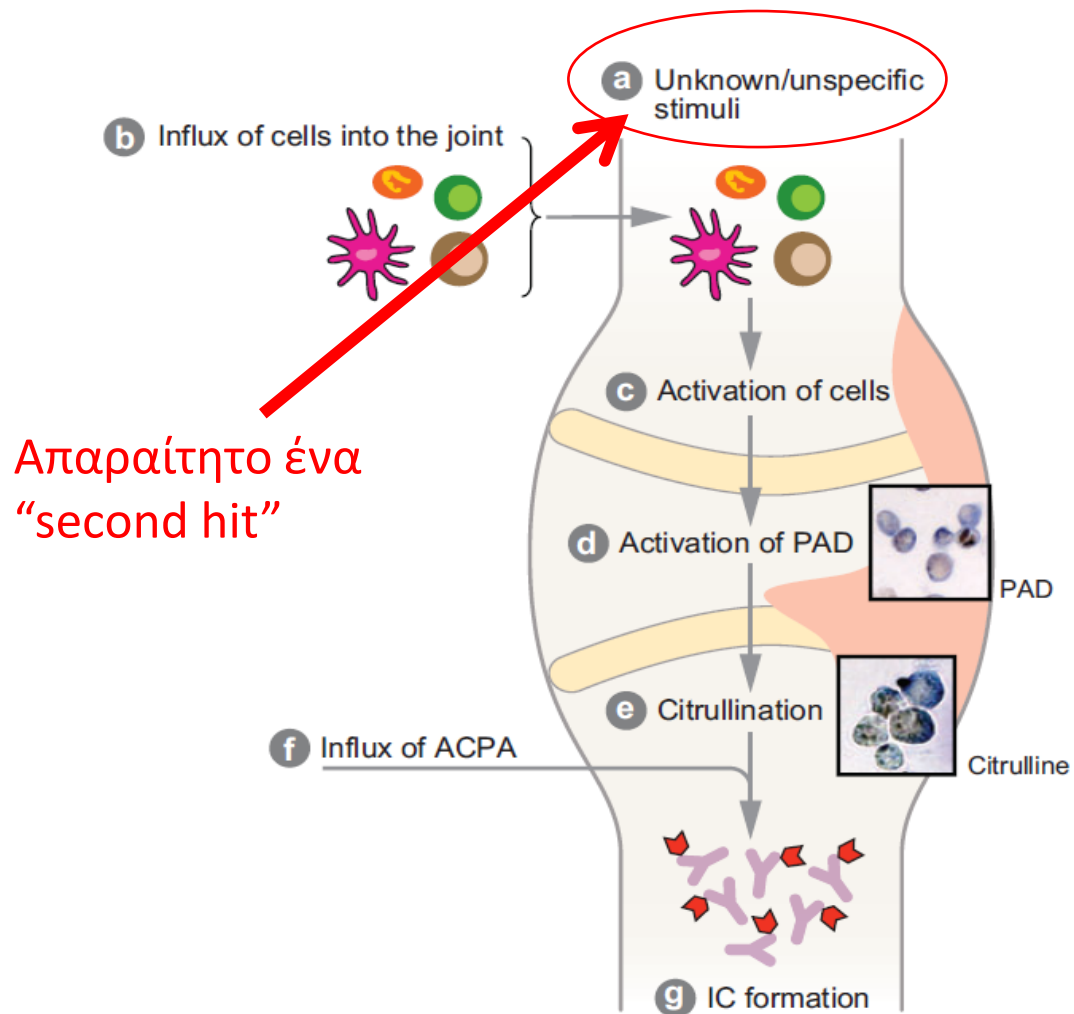
## Stage 1: Immune response



# Πως προσβάλλονται οι αρθρώσεις?

Stage 2:  
Pathologic inflammatory response

Stage 3:  
Chronic rheumatoid arthritis



Απαραίτητο ένα  
"second hit"

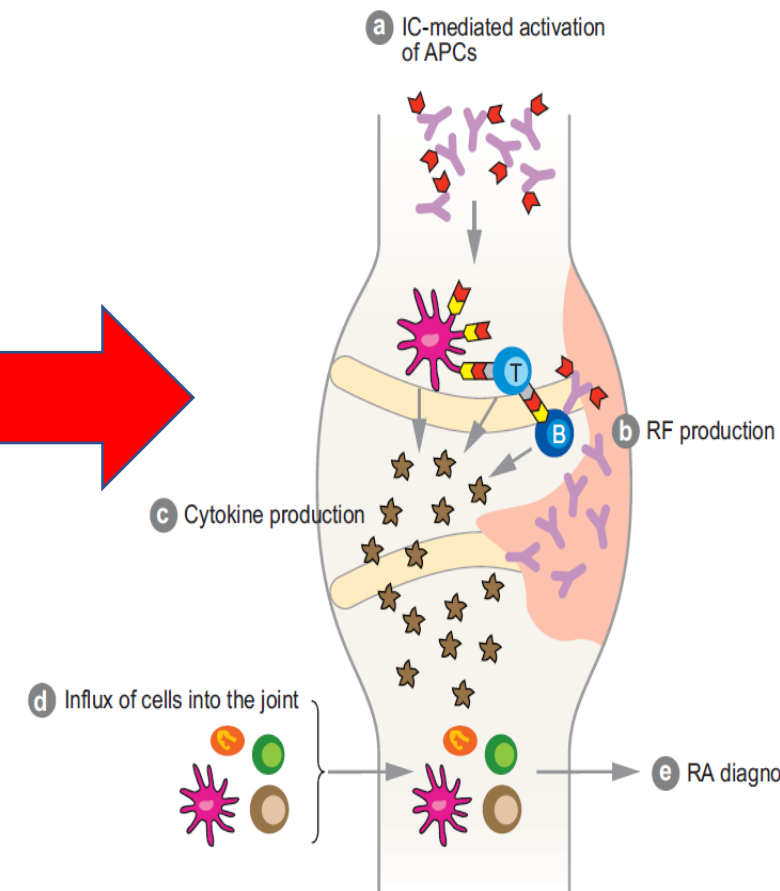
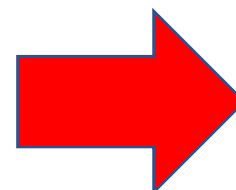
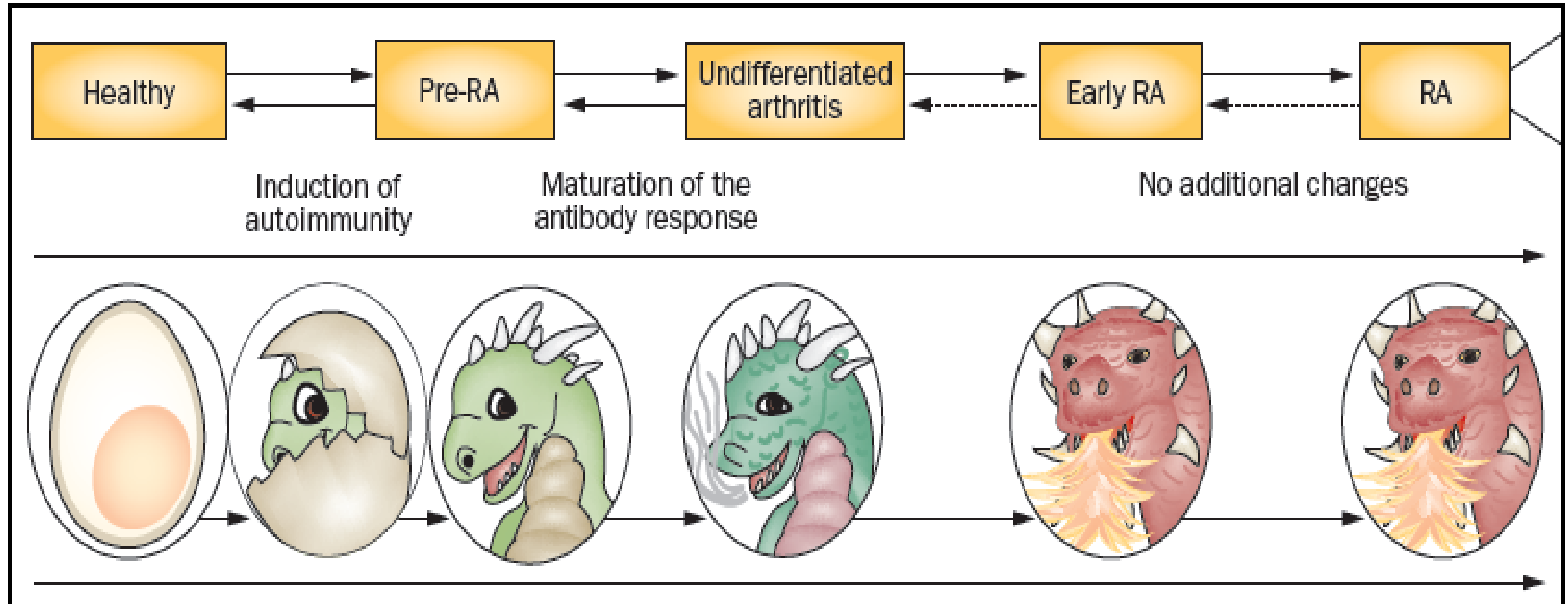
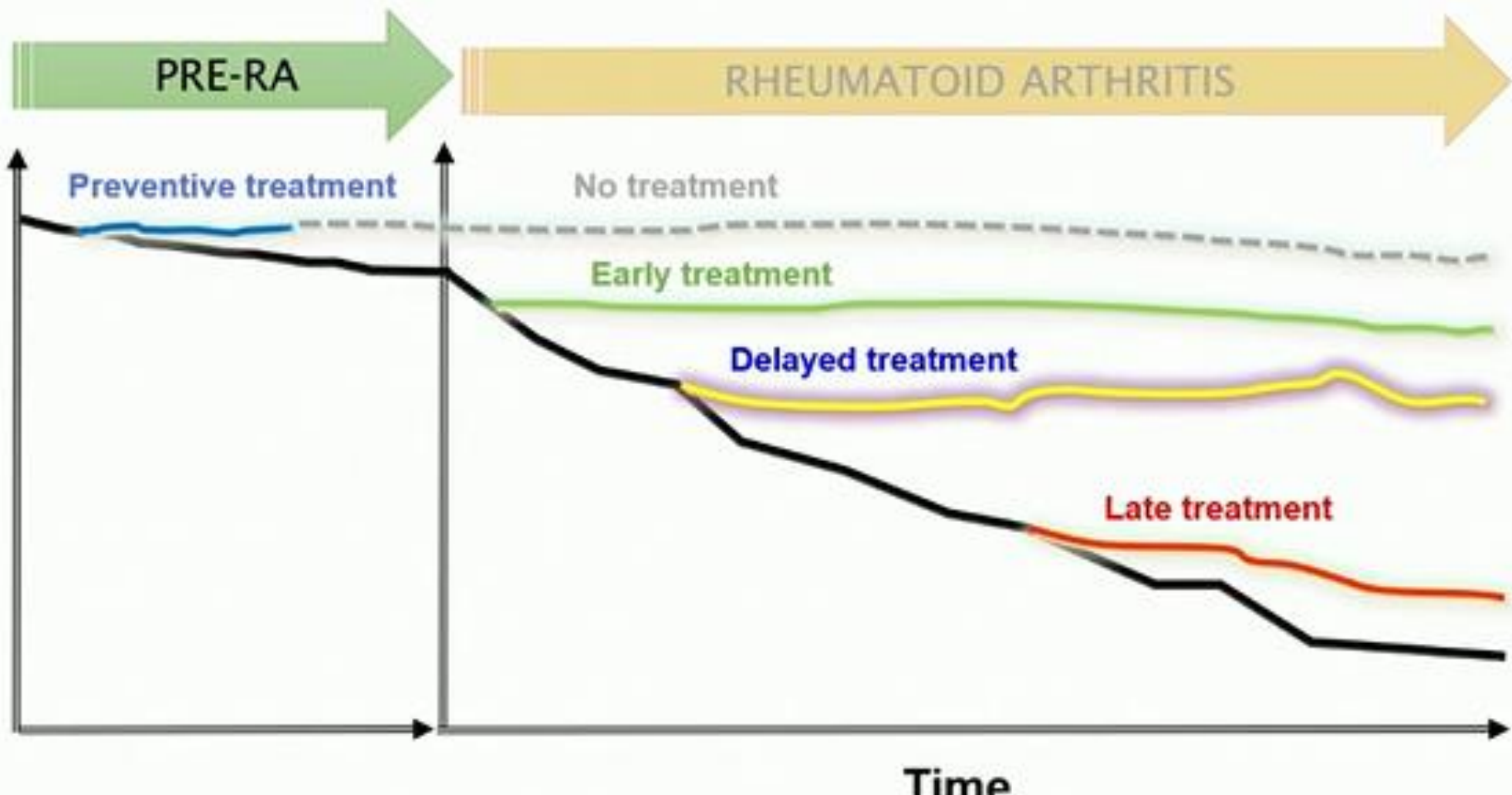


Figure 5

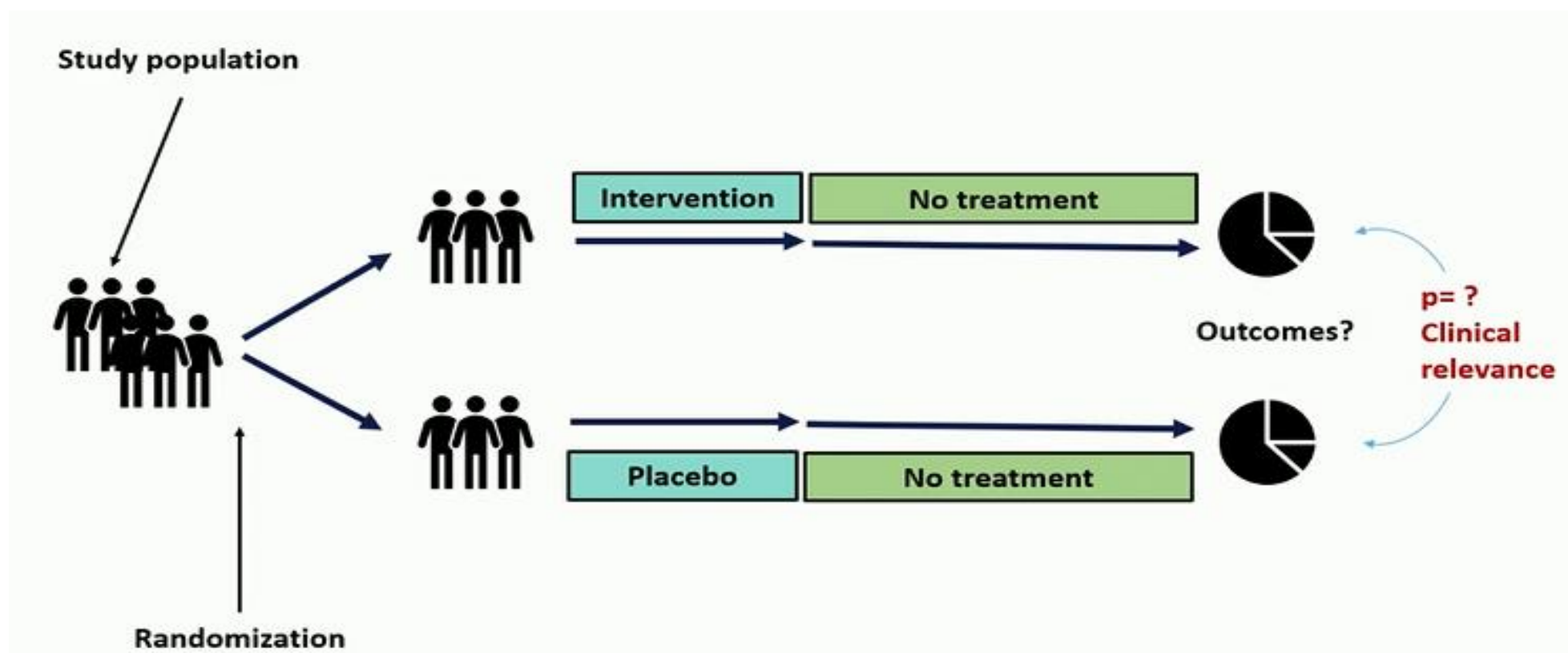
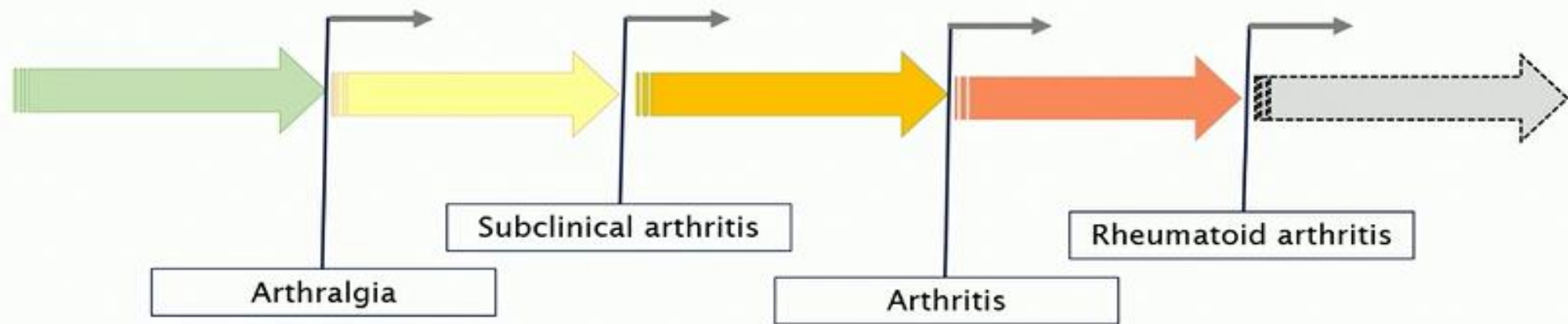
# Η εξέλιξη της ανοσολογικής απόκρισης (σε επίπεδο αυτοαντισωμάτων)











## EULAR definition of arthralgia at risk for RA

### History taking:

- ▶ Joint symptoms of recent onset (duration <1 year)
- ▶ Symptoms located in MCP joints
- ▶ Duration of morning stiffness  $\geq 60$  min
- ▶ Most severe symptoms present in the early morning
- ▶ Presence of a first-degree relative with RA

### Physical examination:

- ▶ Difficulty with making a fist
- ▶ Positive squeeze test of MCP joints



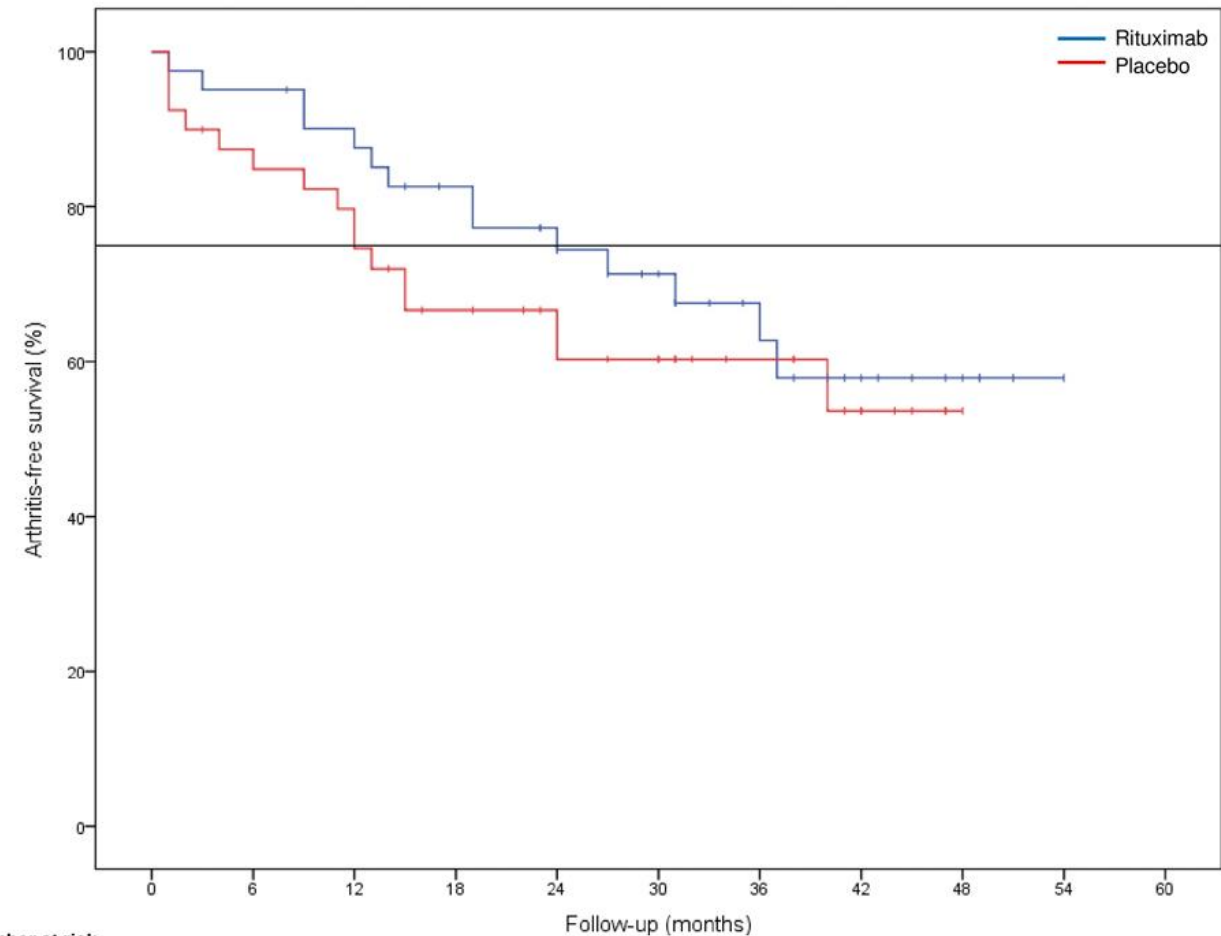
OPEN ACCESS

CLINICAL SCIENCE

## Effects of B-cell directed therapy on the preclinical stage of rheumatoid arthritis: the PRAIRI study

Danielle M Gerlag,<sup>1,2</sup> Mary Safy,<sup>1</sup> Karen I Maijer,<sup>1</sup> Man Wai Tang,<sup>1</sup> Sander W Tas,<sup>1</sup> Mirian J F Starmans-Kool,<sup>3</sup> Astrid van Tubergen,<sup>4</sup> Matthijs Janssen,<sup>5</sup> Maria de Hair,<sup>1</sup> Monika Hansson,<sup>6</sup> Niek de Vries,<sup>1</sup> Aeilko H Zwinderman, Paul P Tak<sup>1</sup>

- Οροθετικοί ασθενείς με αρθραλγίες αλλά **ΌΧΙ** αρθριτιδα
- RTX (1gr) vs placebo

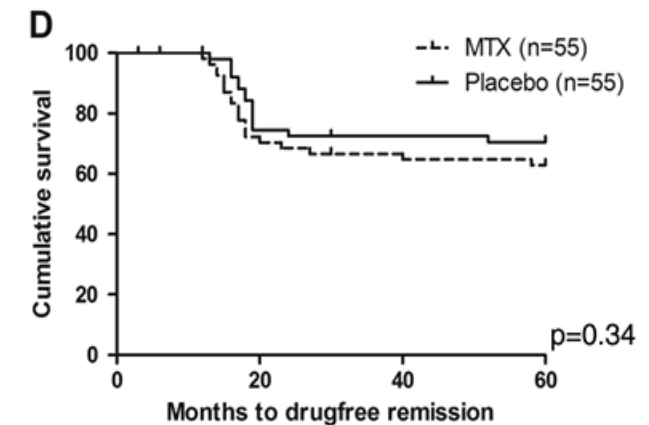
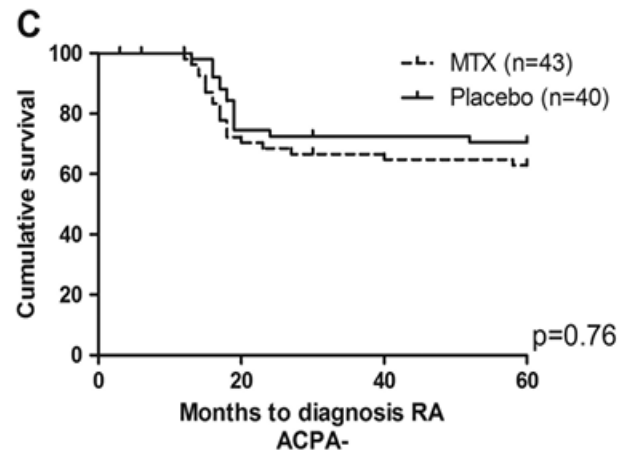
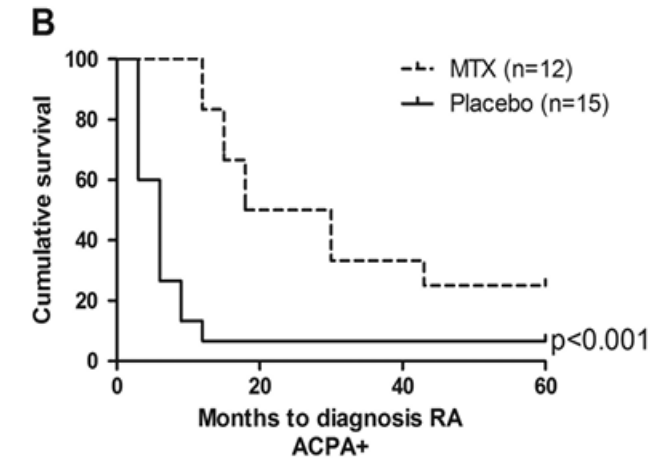
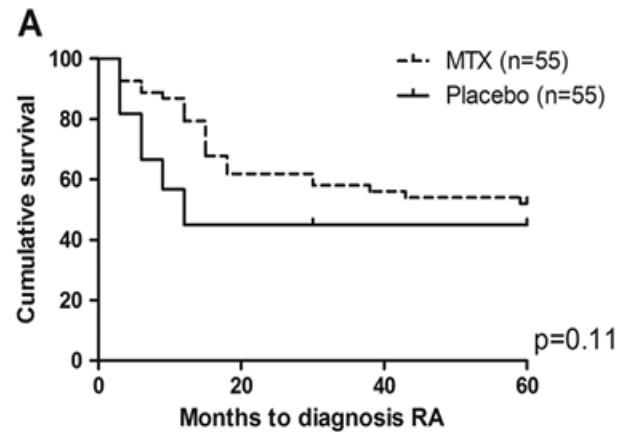


## Five-year outcomes of probable rheumatoid arthritis treated with methotrexate or placebo during the first year (the PROMPT study)

Jill van Aken<sup>1</sup>, Lotte Heimans<sup>1</sup>, Henrike Gillet-van Dongen<sup>1</sup>, Karen Visser<sup>1</sup>, H Karel Ronda<sup>2</sup>, Irene Speyer<sup>3</sup>, André J Peeters<sup>4</sup>, Tom WJ Huizinga<sup>1</sup>, Cornelia F Allaart<sup>1</sup>

Correspondence to Lotte Heimans, Department of Rheumatology, Leiden University Medical Center, PO Box 9600, Leiden 2300 RC, The Netherlands; l.heimans@lumc.nl

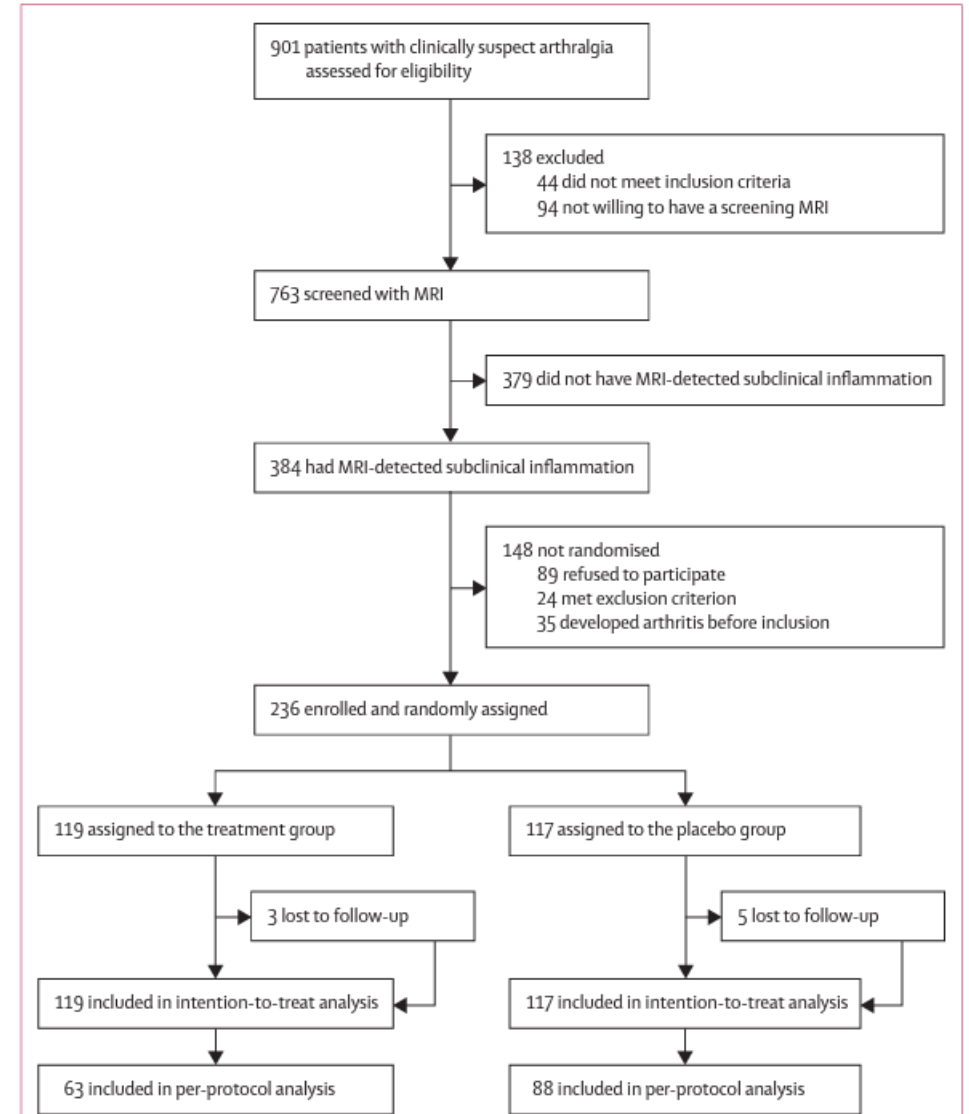
- Ασθενείς με αδιαφοροποίητη αρθρίτιδα και συμπτώματα < 2 ετη
- MTX vs placebo
- Αξιοσημείωτο
  - 25% των ασθενών (κατά βάση οροαρνητικών) δεν ανέπτυξαν ποτέ ΡΑ



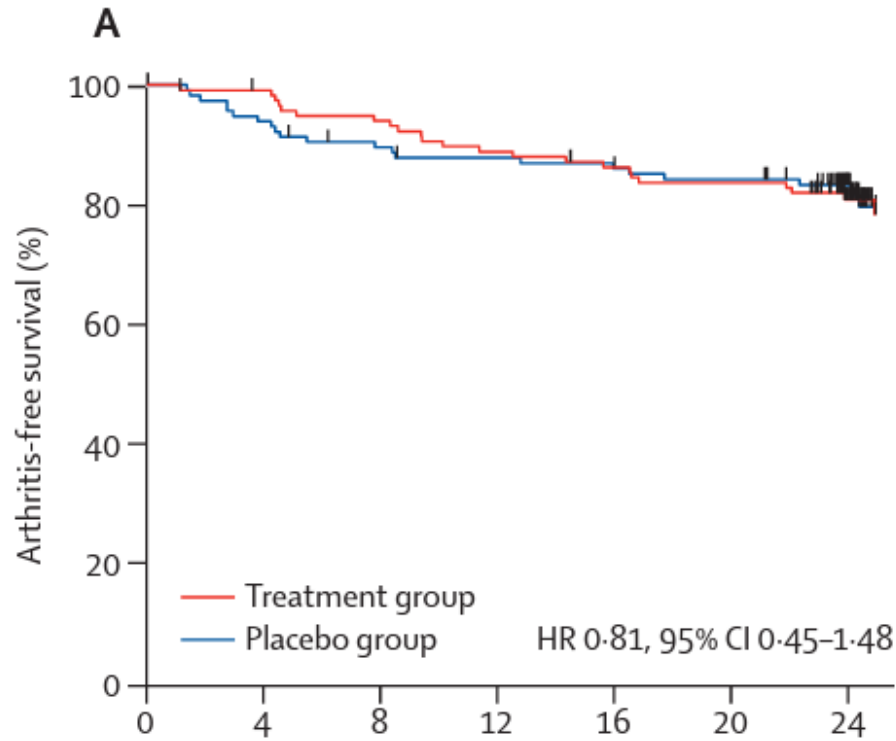
# Intervention with methotrexate in patients with arthralgia at risk of rheumatoid arthritis to reduce the development of persistent arthritis and its disease burden (TREAT EARLIER): a randomised, double-blind, placebo-controlled, proof-of-concept trial

*Doortje I Krijbolder, Marloes Verstappen, Bastiaan T van Dijk, Yousra J Dakkak, Leonie E Burgers, Aleid C Boer, Yune Jung Park, Marianne E de Witt-Luth, Karen Visser, Marc R Kok, Esmeralda T H Molenaar, Pascal H P de Jong, Stefan Böhringer, Tom W J Huizinga, Cornelia F Allaart, Ellis Niemantsverdriet, Annette H M van der Helm-van Mil*

- Ασθενείς με αρθραλγίες και ευρήματα στην μαγνητική
- IM στεροειδές (120mg) και MTX vs placebo για 1 έτος



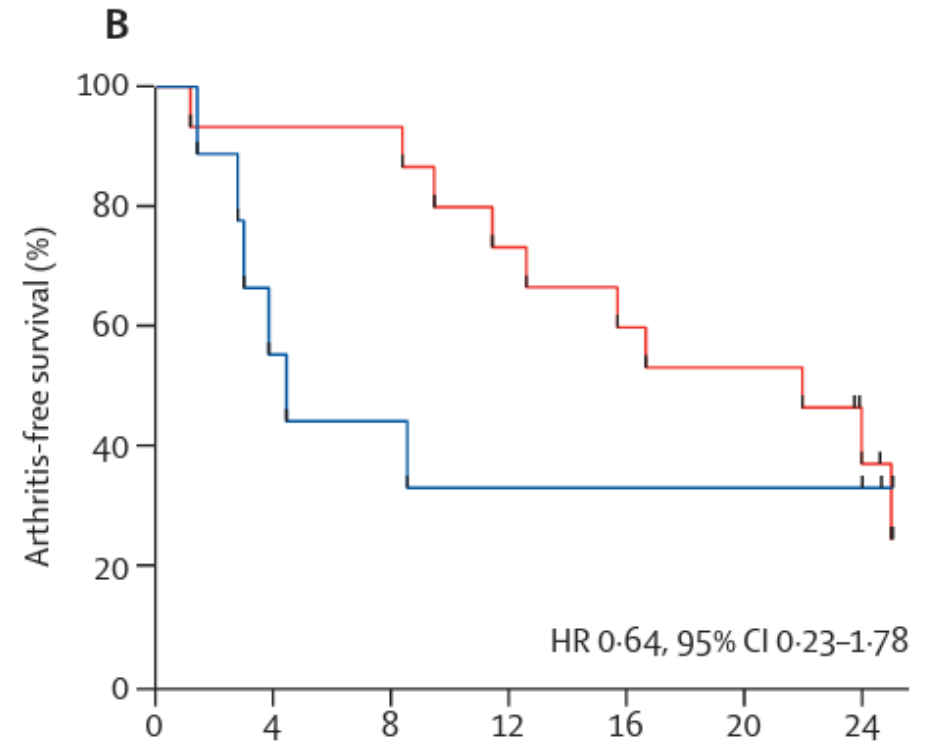
# Total population



**Number at risk  
(number with event)**

Treatment group	119 (0)	116 (1)	110 (7)	104 (13)	100 (16)	97 (19)	32 (23)
Placebo group	117 (0)	109 (7)	102 (12)	99 (14)	98 (15)	94 (18)	39 (21)

# High risk for progression (ACPA+/subclinical joint inflammation)



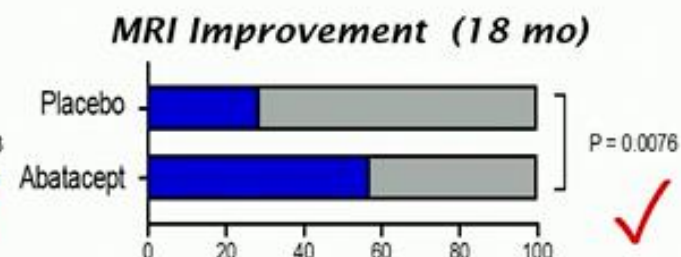
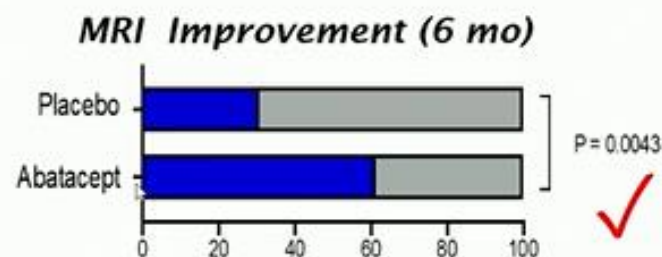
**Number at risk  
(number with event)**

Treatment group	15 (0)	15 (1)	14 (1)	11 (4)	9 (6)	7 (8)	2 (10)
Placebo group	9 (0)	5 (4)	4 (5)	3 (6)	3 (6)	3 (6)	2 (6)

# Προσπάθειες με το abatacept....

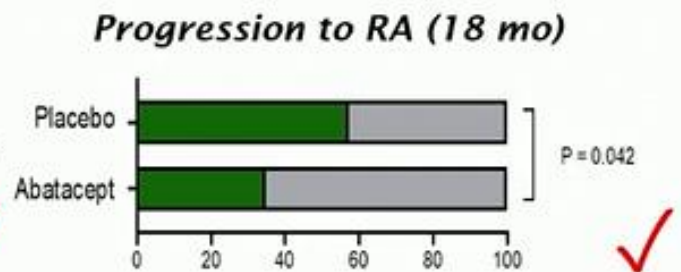
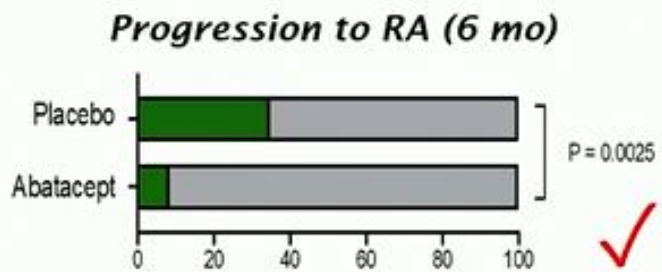
ARIAA: RCT Placebo vs. ABA in RA at risk  
6 months treatment phase + 12 months observation phase

**PCB**  
30%  
61%  
**ABA**



**PCB**  
28%  
57%  
**ABA**

**PCB**  
34%  
8%  
**ABA**



**PCB**  
57%  
34%  
**ABA**

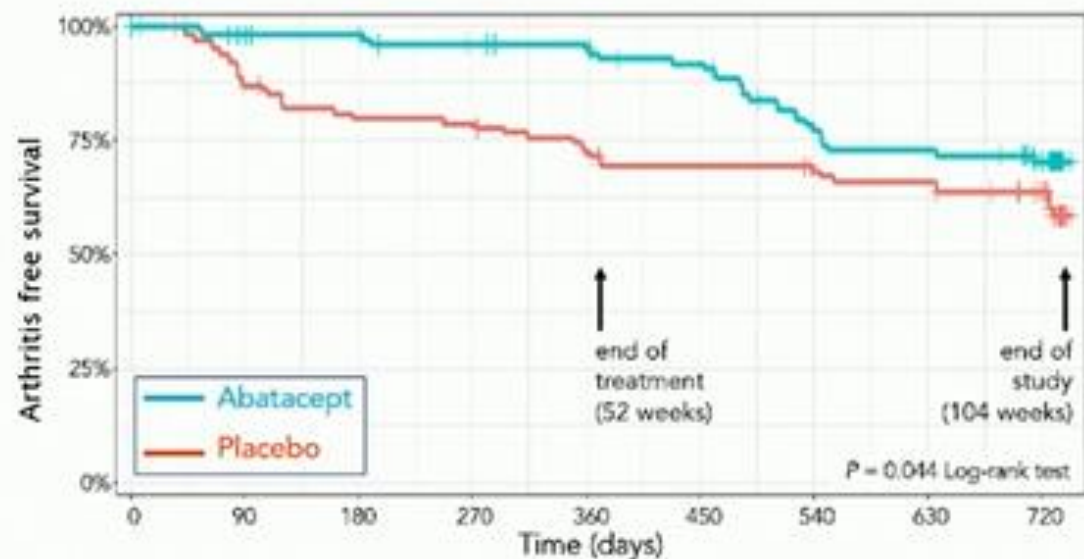


# Treatment of RA before the diagnosis

## Abatacept: the APIPPRA Study

“Arthritis Prevention In The Pre-clinical Phase Of RA with Abatacept”

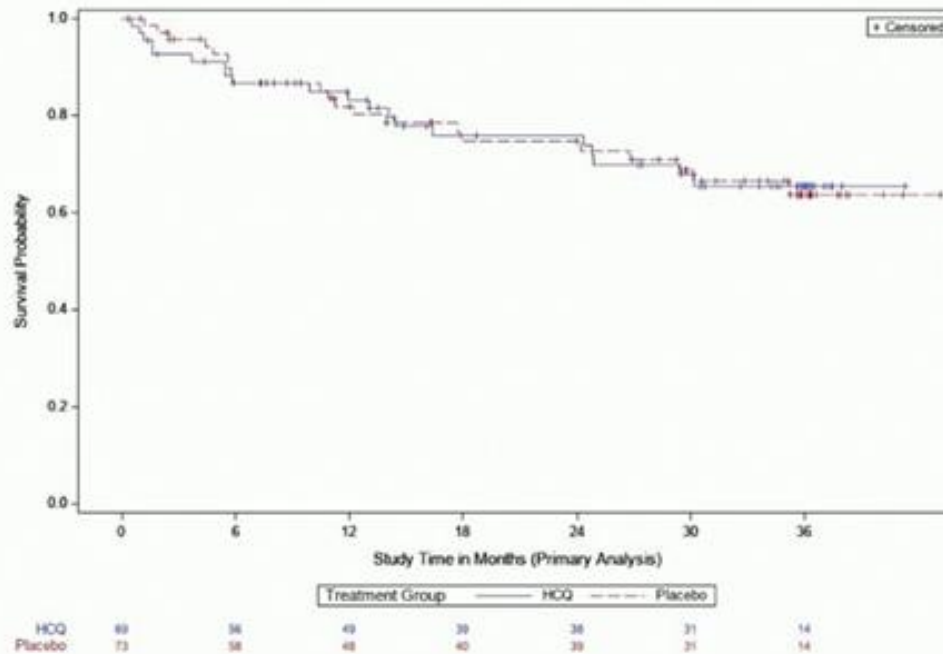
- Arthralgia
- ACPA and RF positive, or high titre ACPA
- Primary outcome: clinical synovitis ( $\geq 3$  joints) or ACR/EULAR 2021
- **Weekly abatacept (125mg) or placebo for 12 months**
- **Results- Primary outcome reached:**
  - 12 months: 29% (PLC) v 6% (ABA)
  - 24 months: 37% (PLC) v 25% (ABA)



	0	90	180	270	360	450	540	630	720	
Number at risk:	103	87	77	76	69	64	61	59	49	Placebo
Cumulative events:	0	13	20	21	27	30	31	33	35	
Cumulative censored obs:	2	5	6	6	7	9	11	11	20	
Number at risk:	110	100	97	92	89	84	69	65	54	Abatacept
Cumulative events:	0	2	2	4	5	8	21	25	27	
Cumulative censored obs:	4	8	11	14	16	18	20	20	32	

# Έχει νόημα η χορήγηση HCQ σε ασυμπτωματικά άτομα με αυτοαντισώματα??

## The Stop-RA Study



### Recruitment:

- Rheumatology clinics
- Testing of first-degree relatives with established RA,
- Health fairs, blood donors, and biobanks.

### Population:

- Elevated anti-CCP3 AB levels of at least 40 units
- No history of inflammatory arthritis

### Randomisation:

- HCQ (200-400 mg a day based on weight) OR (n=69)
- Placebo (n=73)

### Duration:

- 1-year treatment regimen.

# Που καταλήγουμε?

- Δεν αλλάζει τίποτε στην καθημερινή κλινική πράξη
- Θεραπεύουμε την αρθρίτιδα (που βρίσκουμε στην ΦΕ)
- Παρακολουθούμε εντατικά ασθενείς με ύποπτα συμπτώματα
- Ισχυρότερος βιοδείκτης εξέλιξης σε RA τα ACPA
  
- Στο μέλλον????



Ευχαριστώ!

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