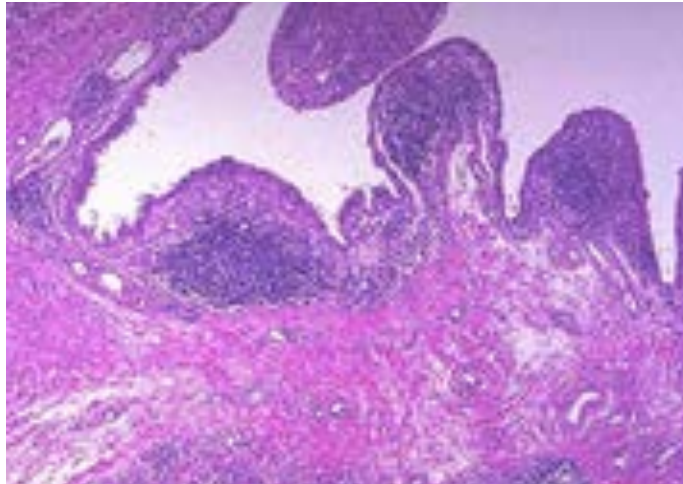


# Rheumatoid arthritis: predicting the diagnosis & preventing damage



Francesca Barone

Senior lecturer

University of Birmingham & Sandwell and West Birmingham Hospitals NHS Trust

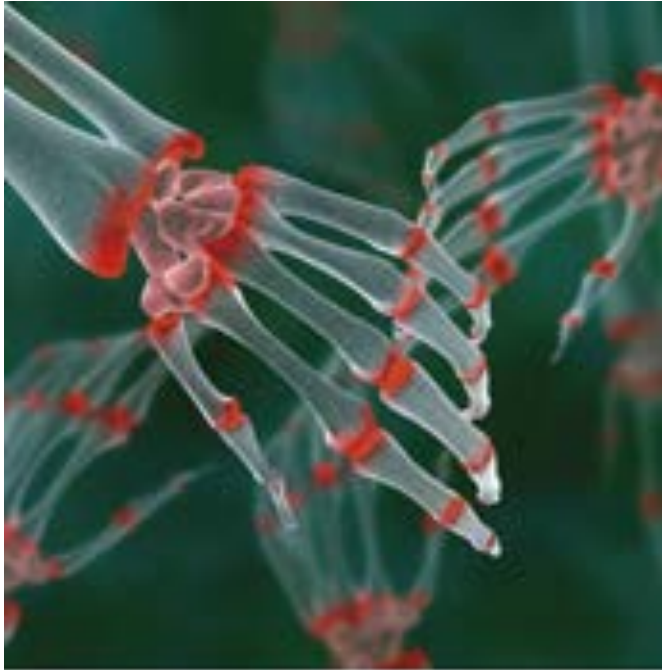


3/31/2016



3/31/2016

# Rheumatoid arthritis



## Common:

580,000 adults have RA in England  
28,000 new cases per year

## Costly:

Annual NHS costs: £560 million  
Annual cost to the economy: £1.8 billion



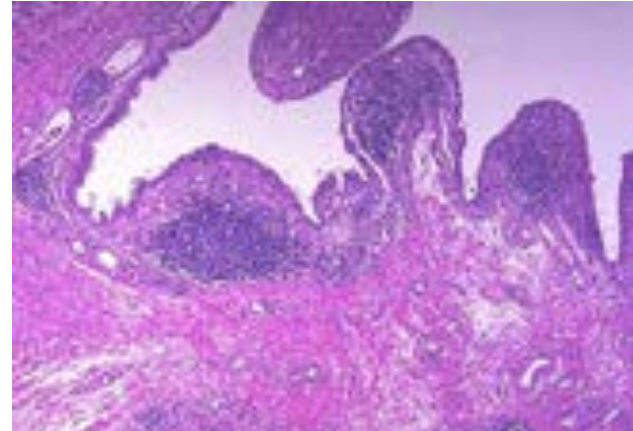
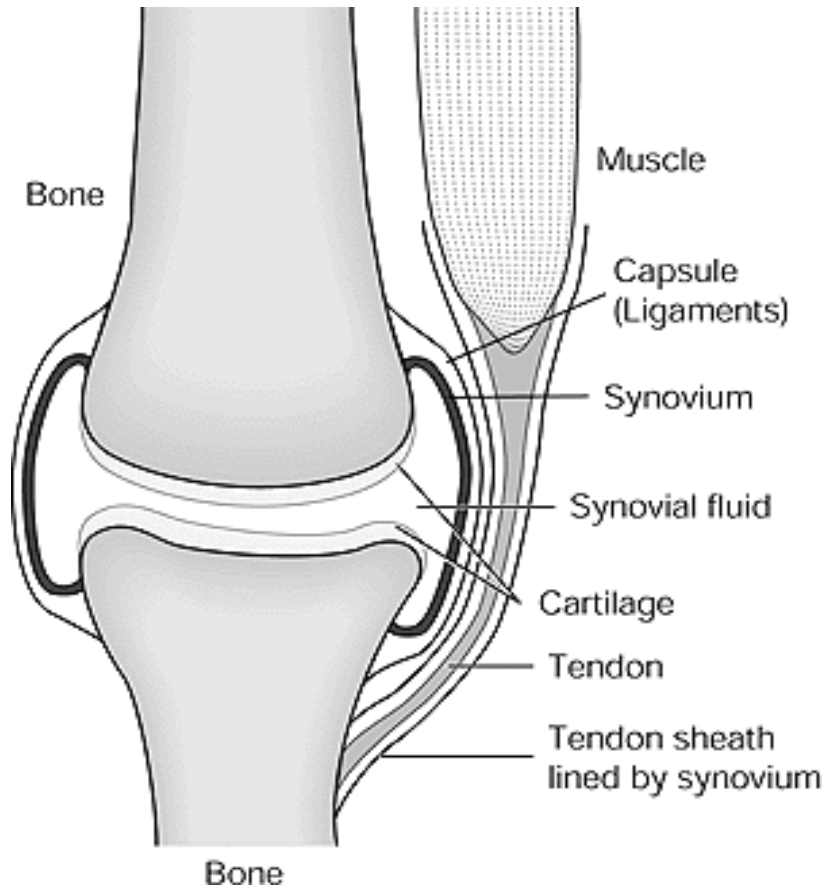
Services for people with rheumatoid arthritis

Report by the Comptroller and Auditor General to the House of Commons and the House of Lords

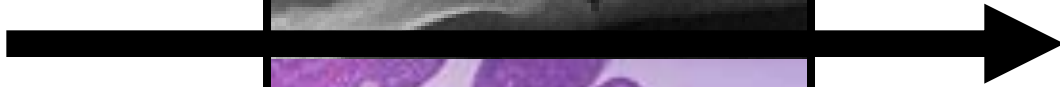
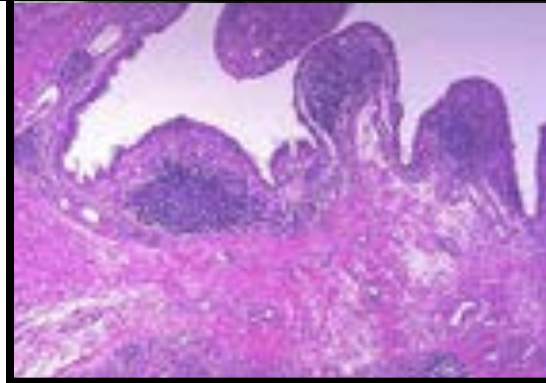
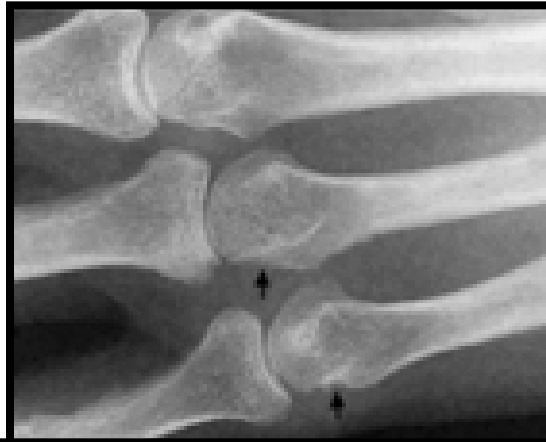


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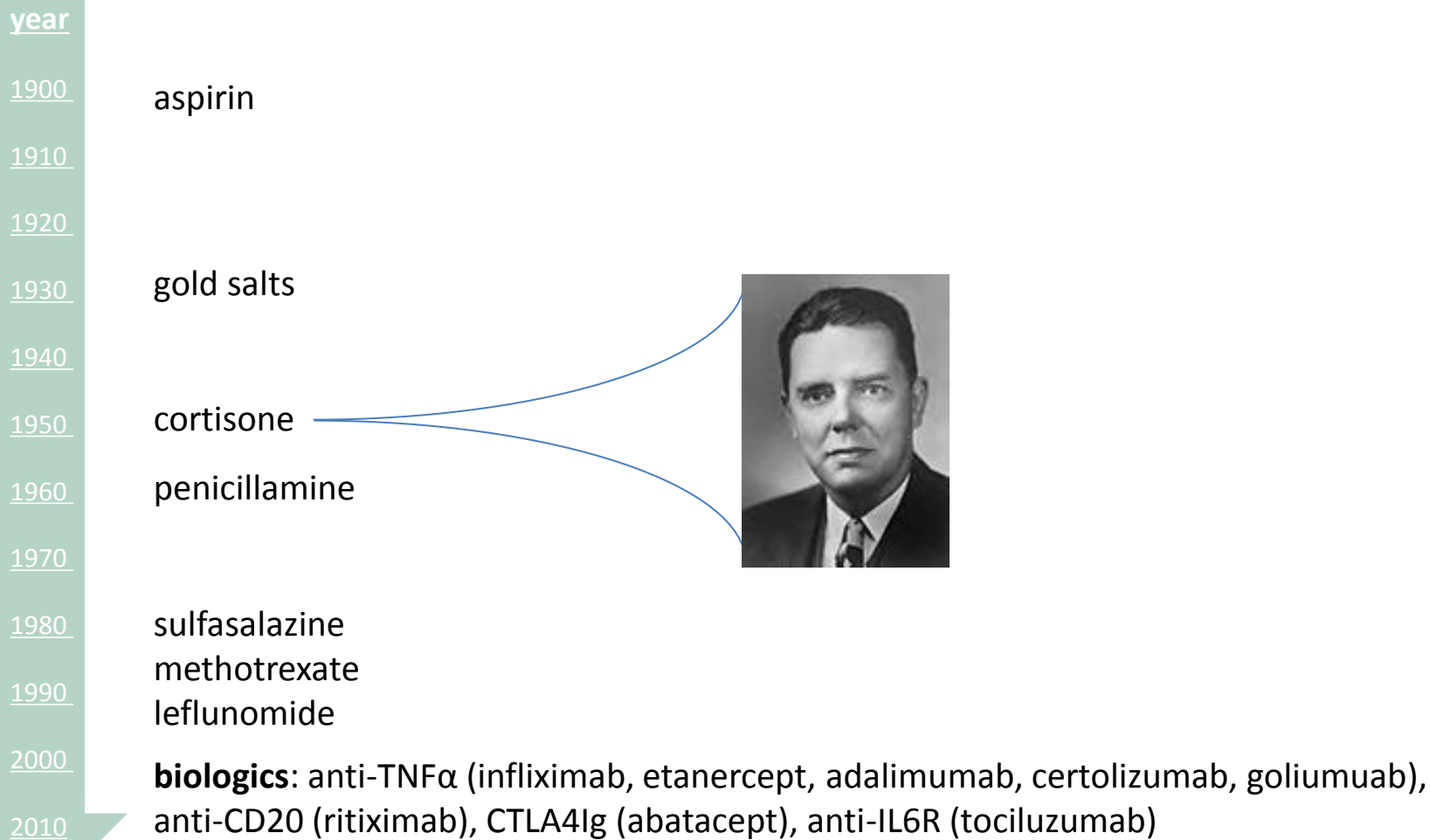
# Synovial inflammation in RA



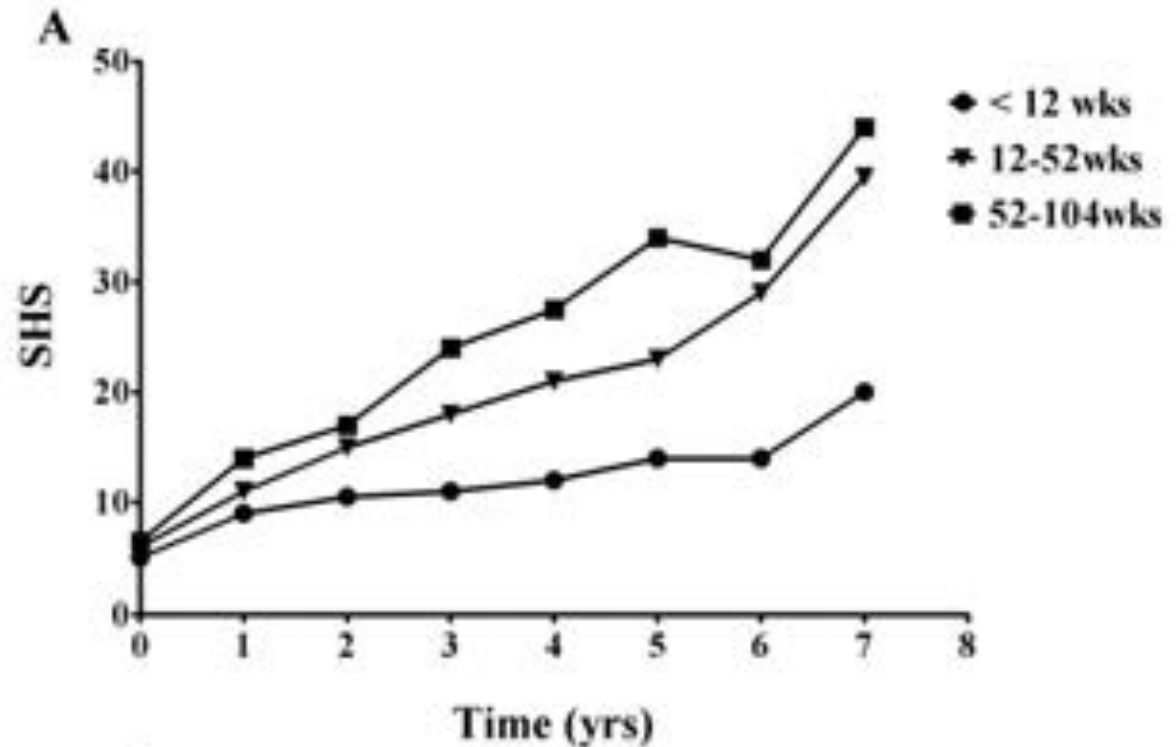
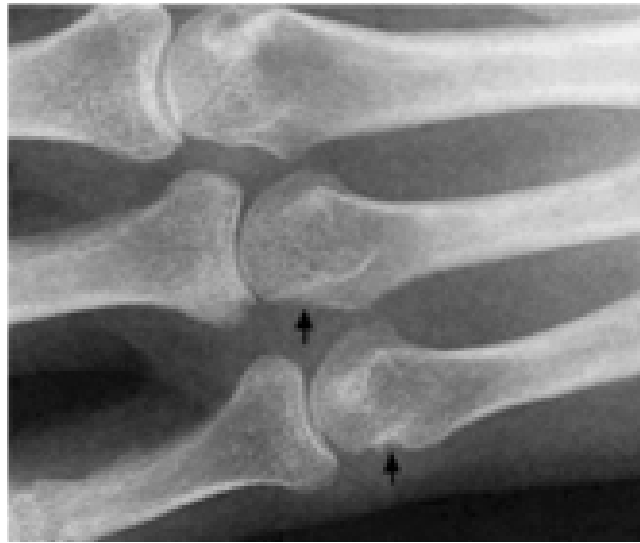
# Synovial inflammation causes damage



*“Almost any drug that has done any good in any other disorder has been tried in the treatment of rheumatoid arthritis, and if faith and optimism are present in either patient or doctor some good results will be obtained for a time in every case, the highest proportion occurring when abundant faith is present in both doctor and patient”* **Frank Dudley Hart**

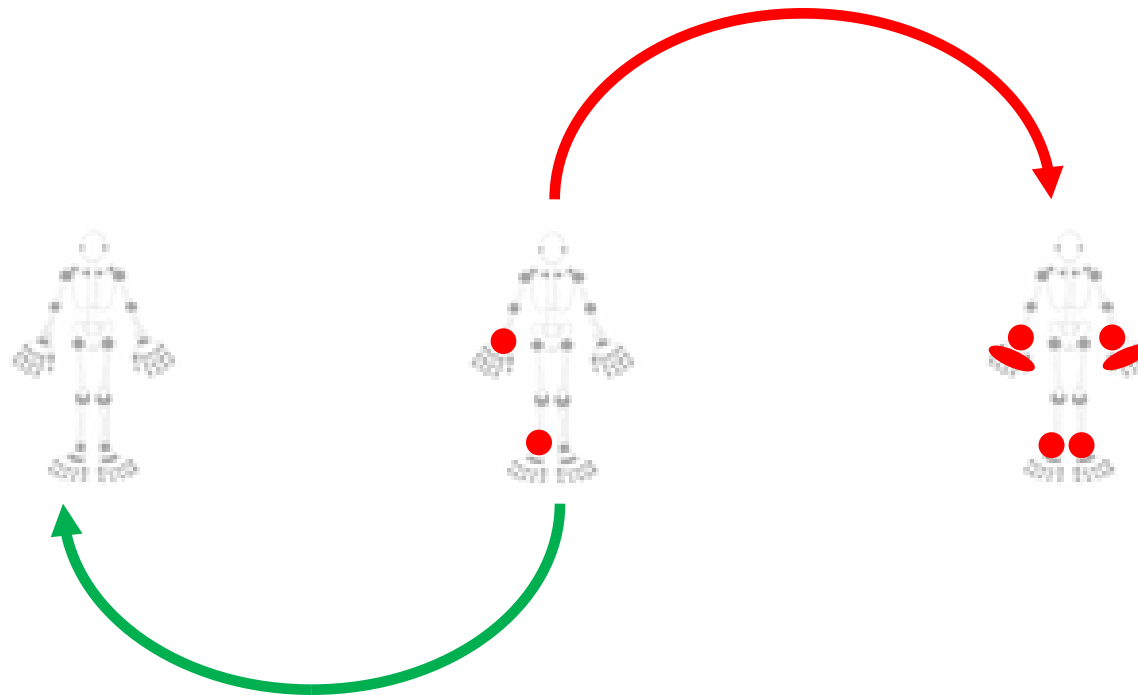


# The impact of delayed treatment

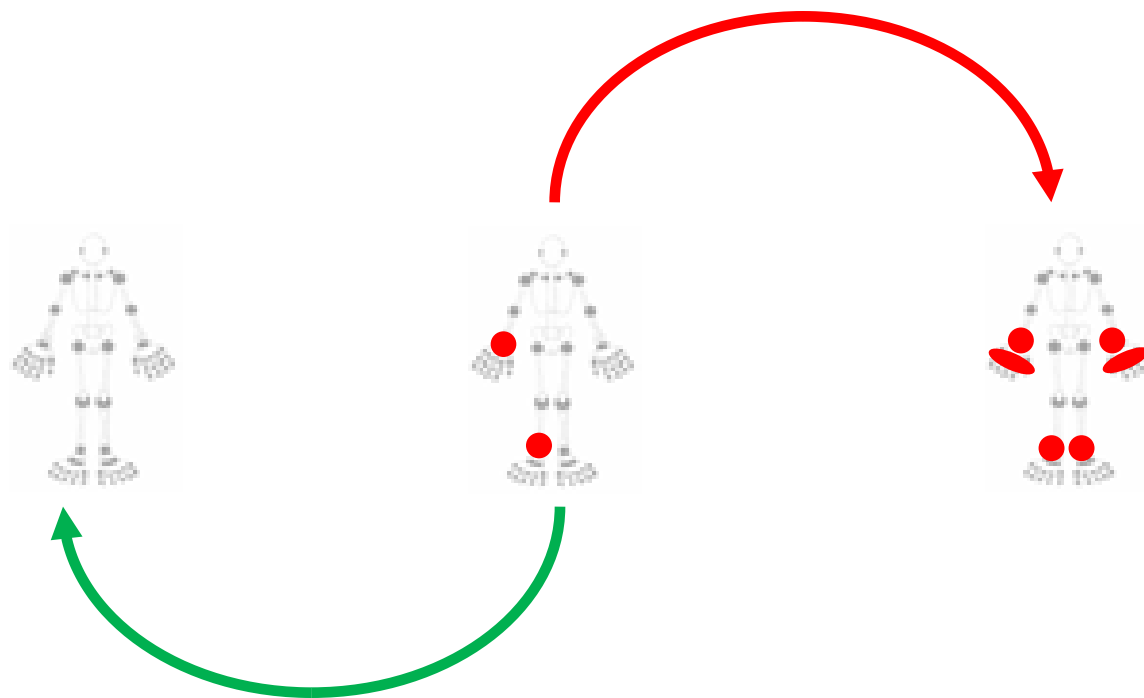


van der Linden M et al. *Arthritis Rheum* 2010

# Inflammatory arthritis is common and not everyone develops RA

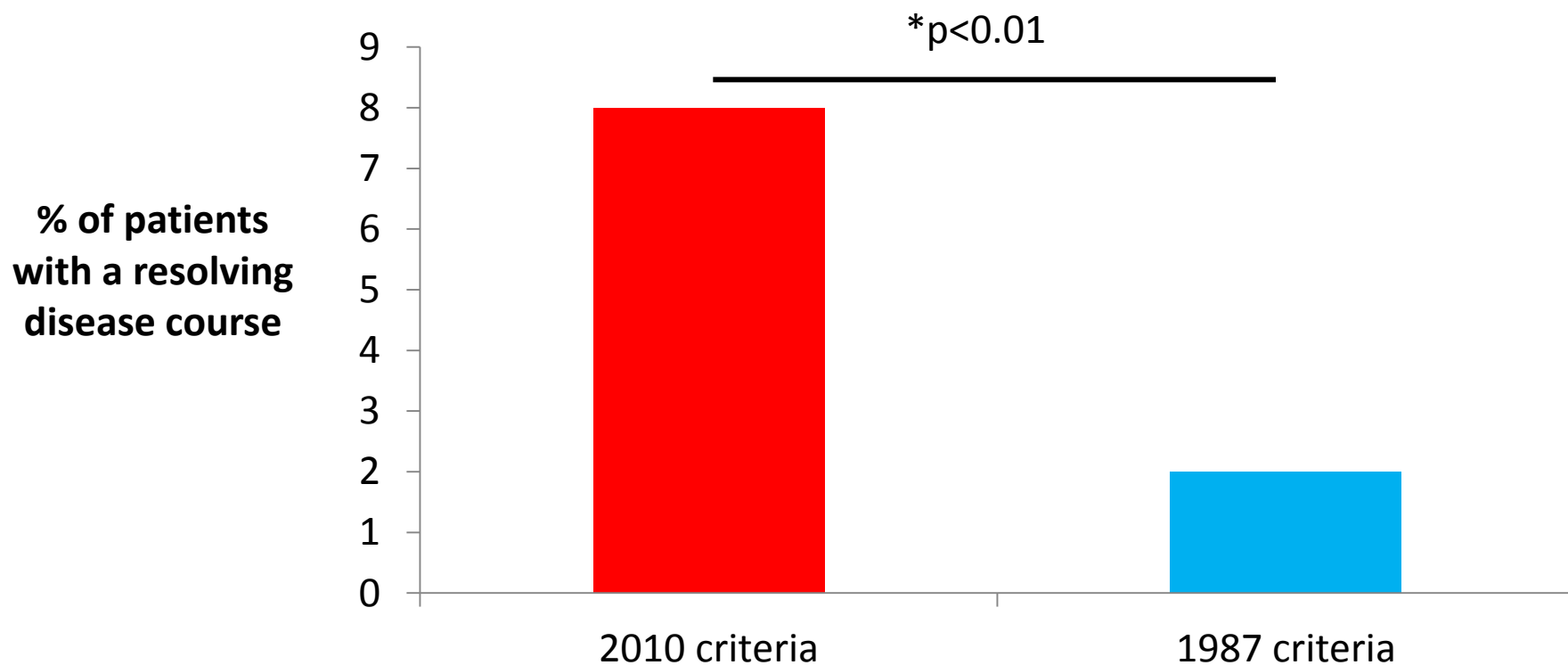






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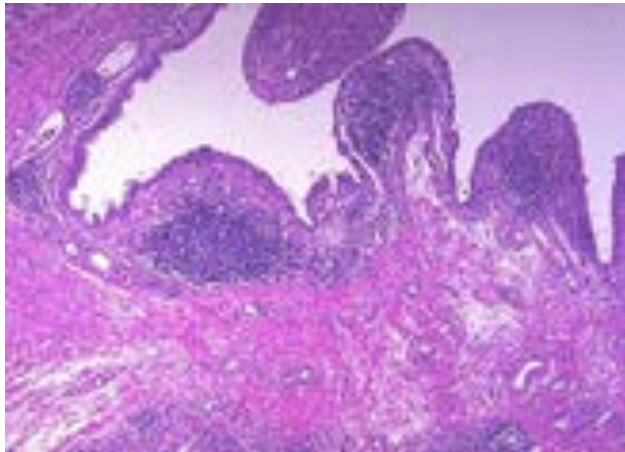
# Classification criteria for RA identify patients whose disease spontaneously resolves



# Autoantibodies

FROM THE PATHOLOGICAL-ANATOMICAL LABORATORY OF  
ULLEVAAL HOSPITAL, OSLO, AND THE BACTERIOLOGICAL  
INSTITUTE OF THE UNIVERSITY OF OSLO.

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ON THE OCCURRENCE OF A FACTOR IN HUMAN  
SERUM ACTIVATING THE SPECIFIC AGGLUTI-  
NATION OF SHEEP BLOOD CORPUSCLES.

By Erik Waaler, M. D.

(Received for publication December 15th, 1939).



# Autoantibodies predict the development of RA in patients with early arthritis

	RF	anti-CCP
<b>Sensitivity</b>	68	68
<b>Specificity</b>	92	96
<b>PPV</b>	68	81
<b>NPV</b>	92	93



Variable		Score
<b>Age (years)</b>		X 0.02
<b>Female</b>		1.0
<b>Joint distribution</b>	small joints hands / feet	0.5
	symmetry	0.5
	upper limbs	1.0
	upper & lower limbs	1.5
<b>Morning stiffness (on 100 VAS)</b>	26-90mm	1.0
	> 90 mm	2.0
<b>Tender joints (n)</b>	4-10	0.5
	> 10	1.0
<b>Swollen joints (n)</b>	4-10	0.5
	> 10	1.0
<b>CRP</b>	5-50	0.5
	>50	1.5
<b>RF +ve</b>		1.0
<b>Anti-CCP Ab +ve</b>		2.0



ARthritis & Rheumatism  
 Vol 49, No. 11, pages 2001-2007  
 2007, American College of Rheumatology

### Validation of a Prediction Rule for Disease Outcome in Patients With Recent-Onset Undifferentiated Arthritis

Moving Toward Individualized Treatment Decision-Making

Antonia H. M. van der Helm-van Mil,<sup>1</sup> Jacqueline Dorst,<sup>2</sup> Saska le Cessie,<sup>1</sup> Andrew Filer,<sup>1</sup> Hans Bartel,<sup>2</sup> Gerd R. Burmester,<sup>2</sup> Tom W. J. Huizinga,<sup>1</sup> and Karin Raza<sup>2</sup>



# The best predictive instrument we have?

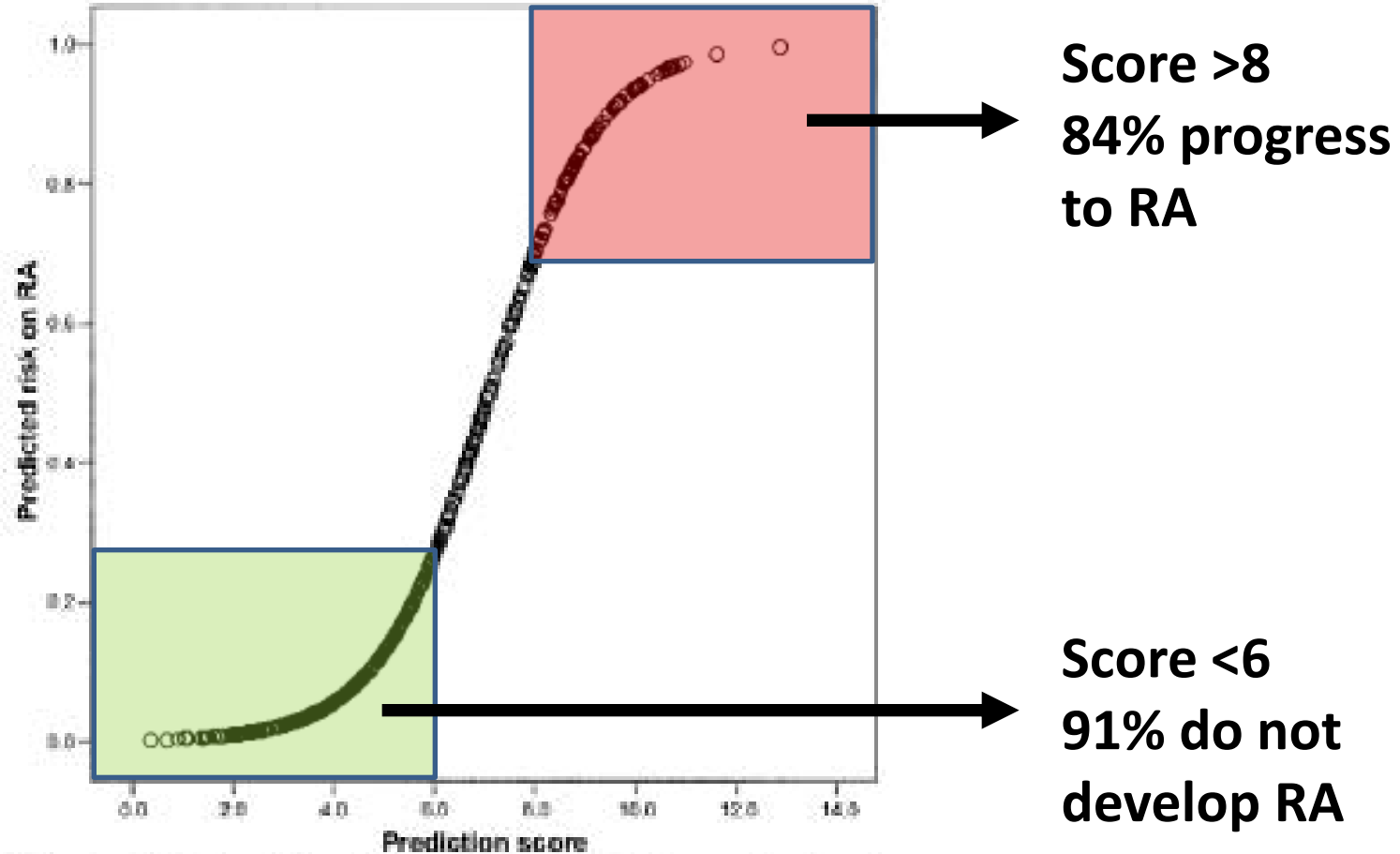


Figure 2. Predicted risk of rheumatoid arthritis (RA) as a function of the prediction score.



# The best predictive instrument we have?

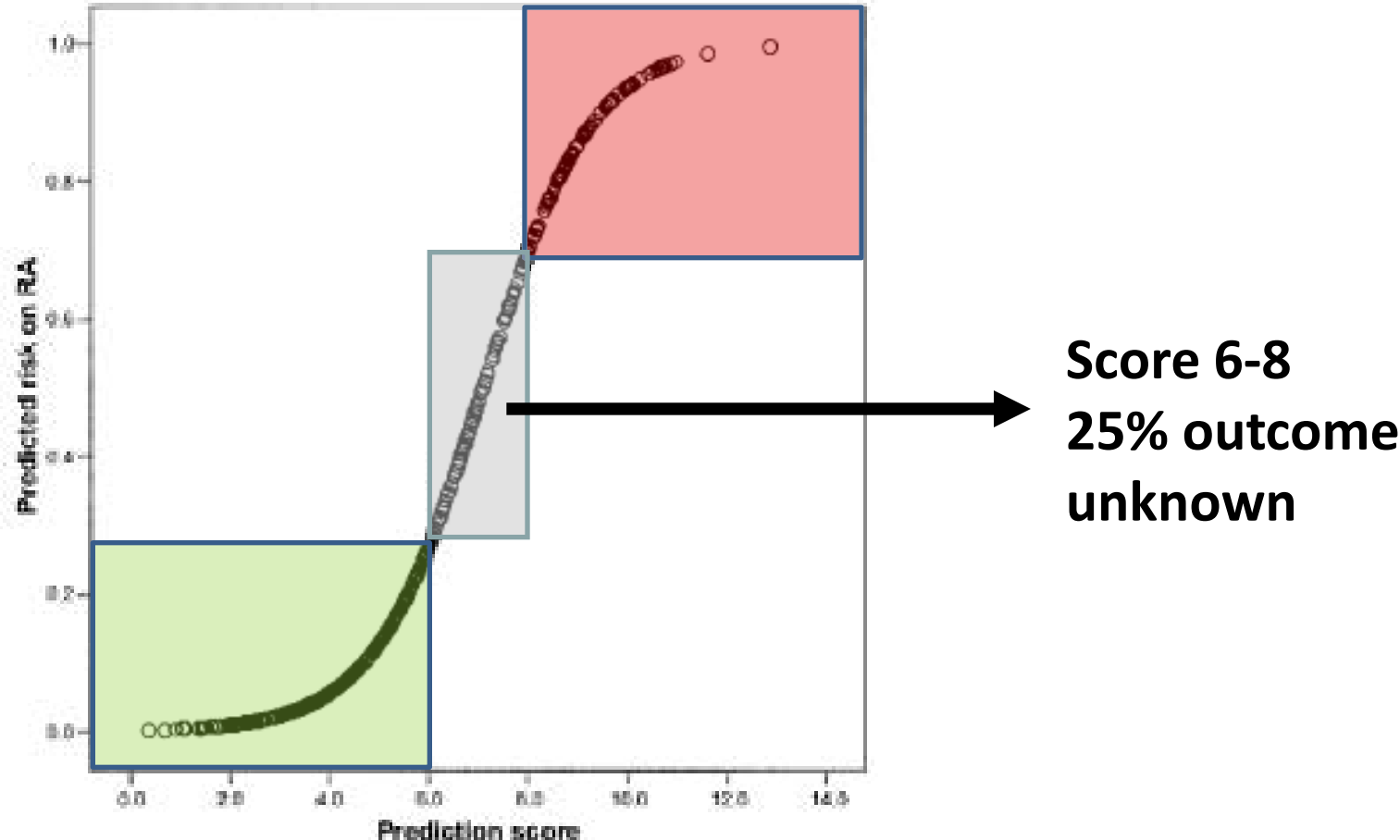
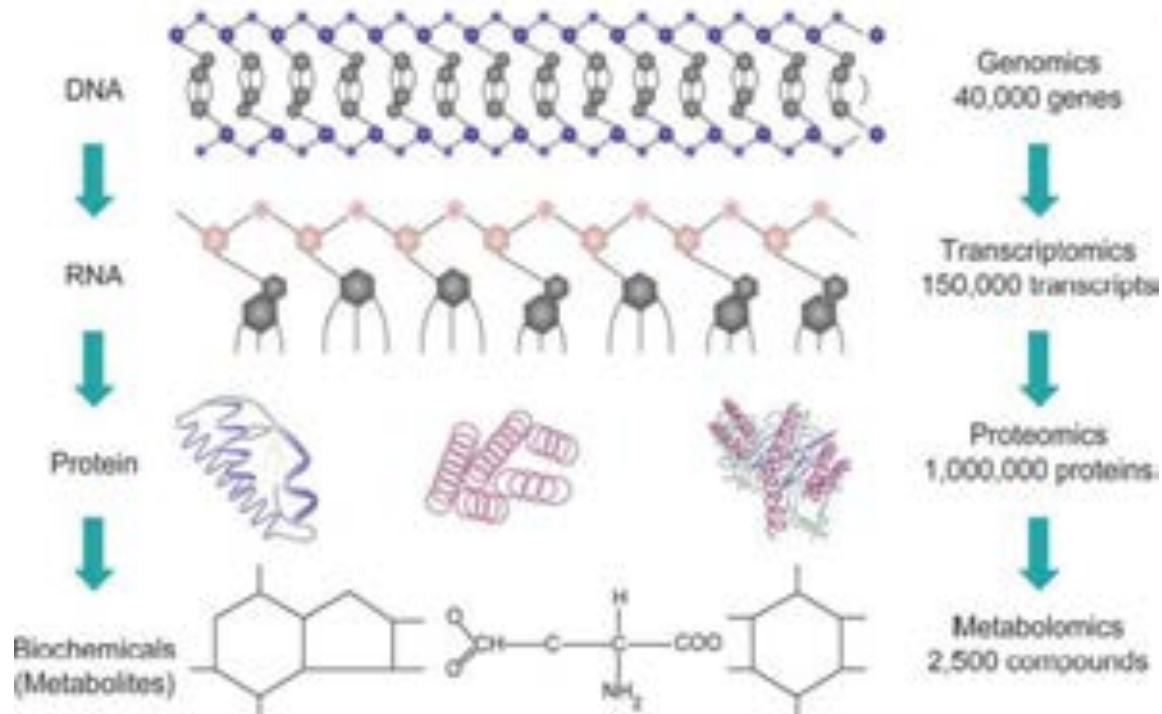


Figure 2. Predicted risk of rheumatoid arthritis (RA) as a function of the prediction score.





# Measuring the metabolome to predict outcome in early arthritis





# Measuring the metabolome to predict outcome in early arthritis

## Risk factors



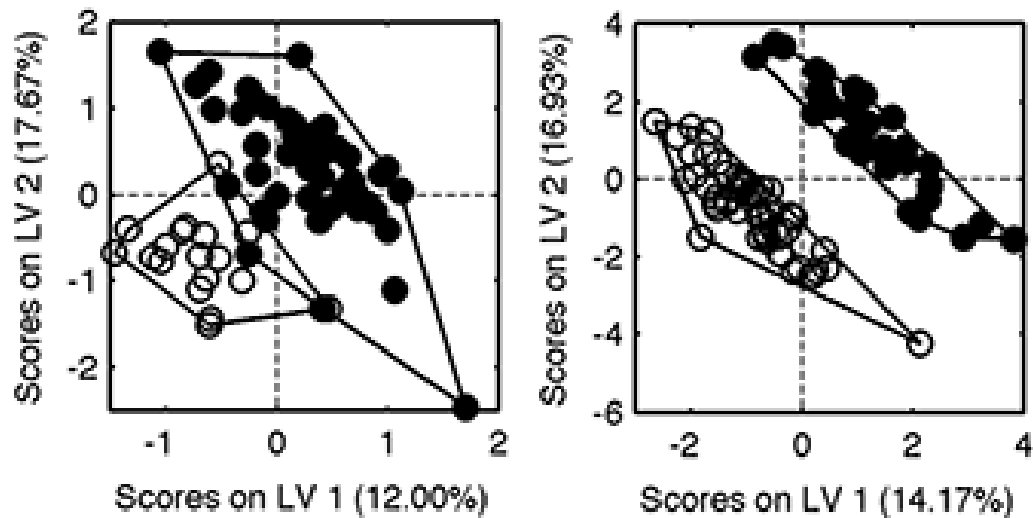
## metabolism



## Inflammation



# The serum metabolome predicts outcome in early arthritis

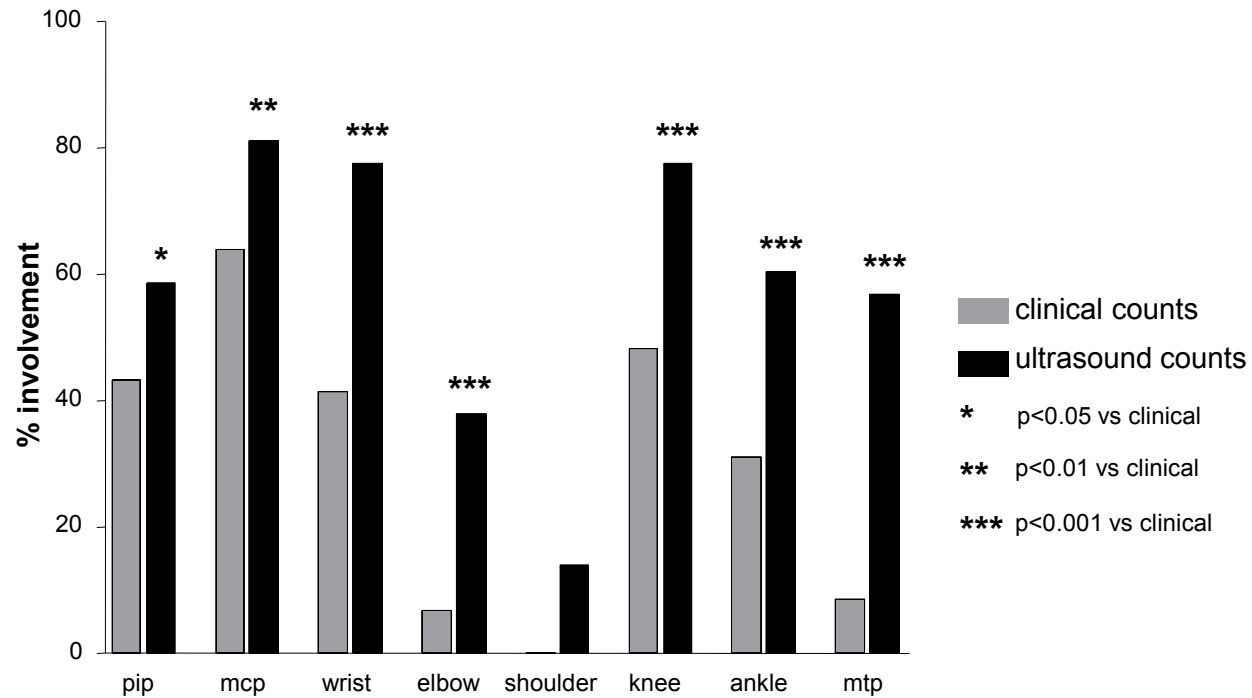
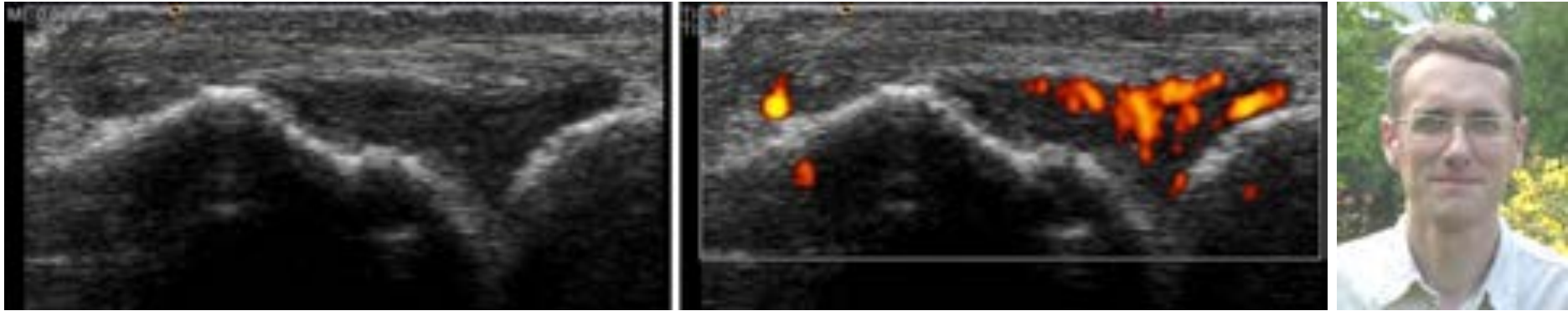


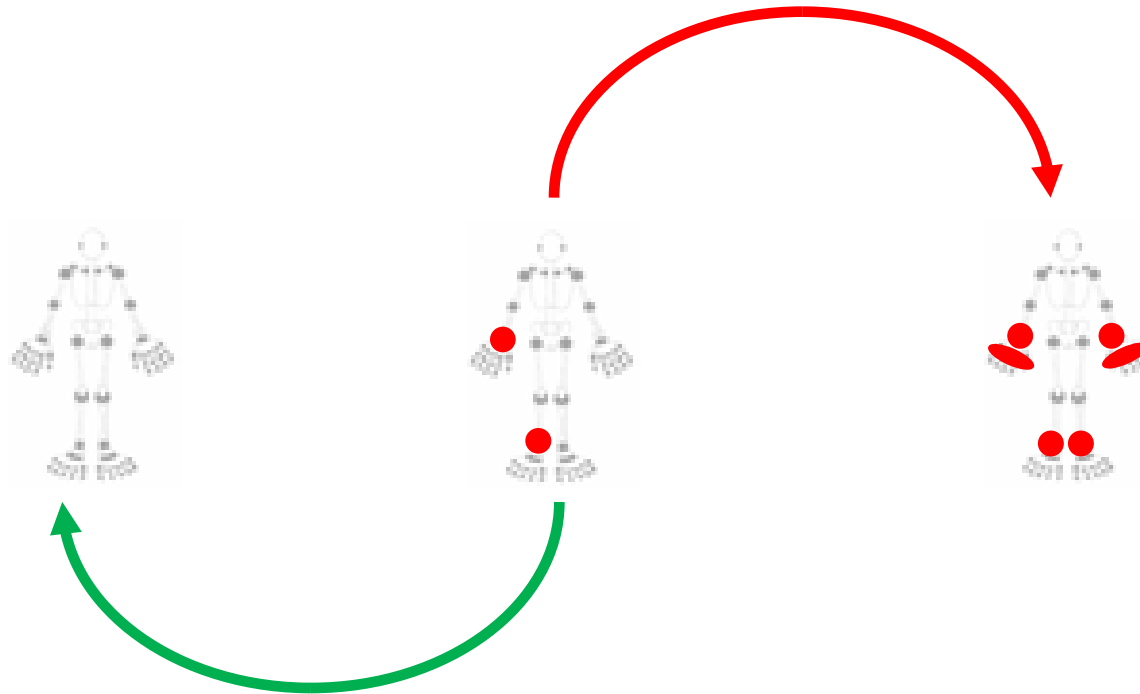
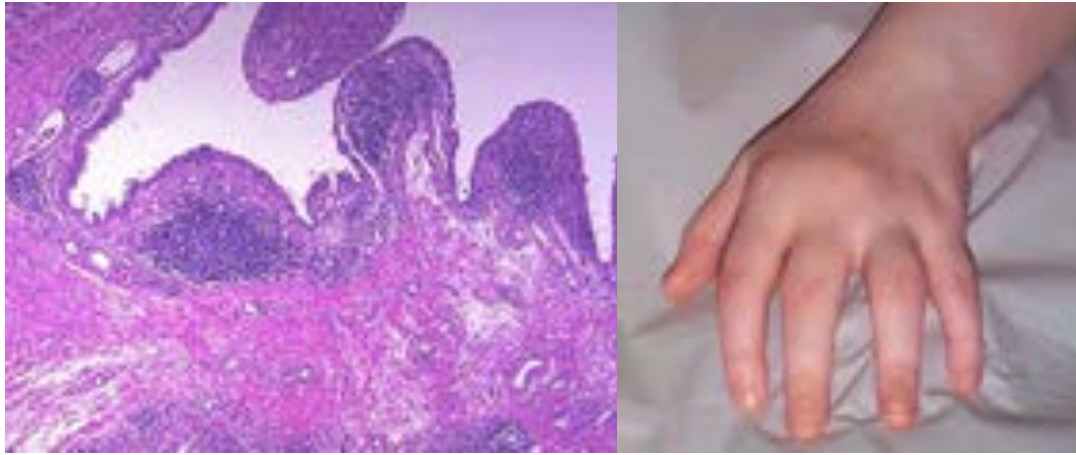
- Resolving arthritis
- Rheumatoid arthritis

# Aiming for better prediction tools

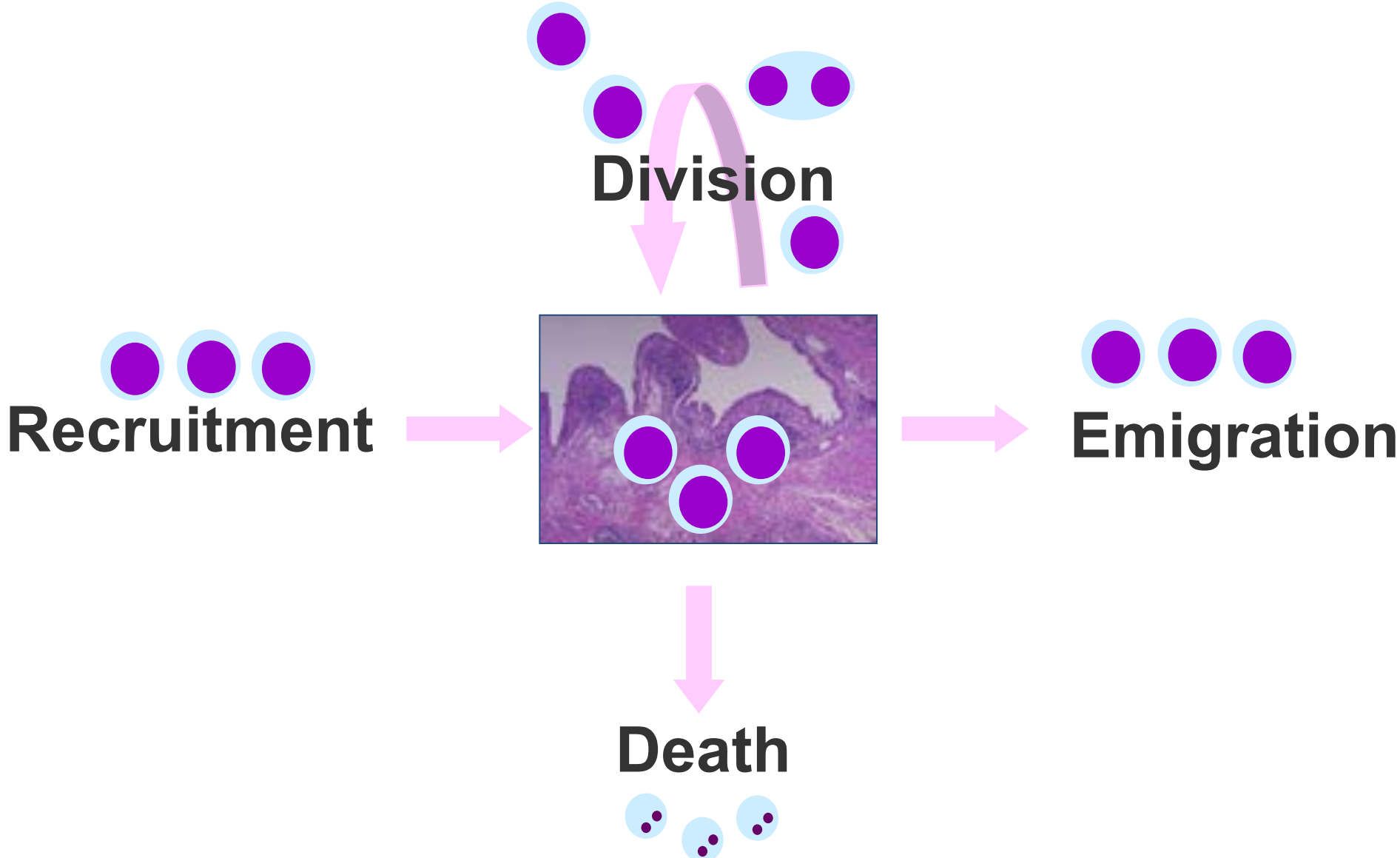
Variable		Score
Age (years)		X 0.02
Female		1.0
<b>Joint distribution</b>	small joints hands / feet	0.5
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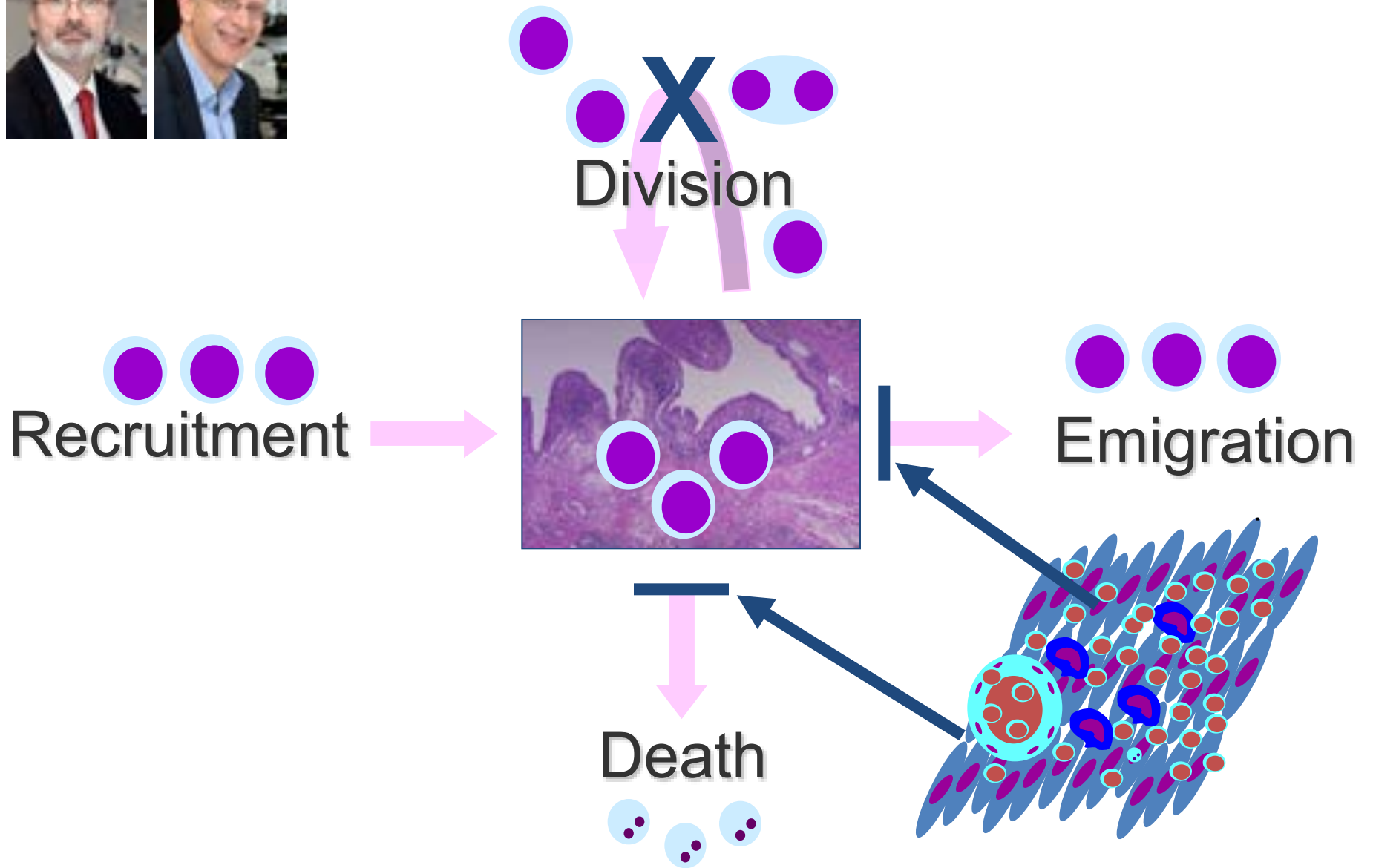
# Ultrasound in very early synovitis



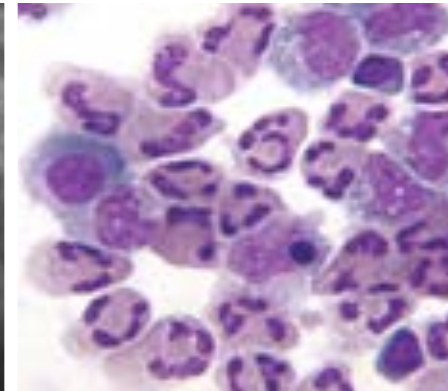
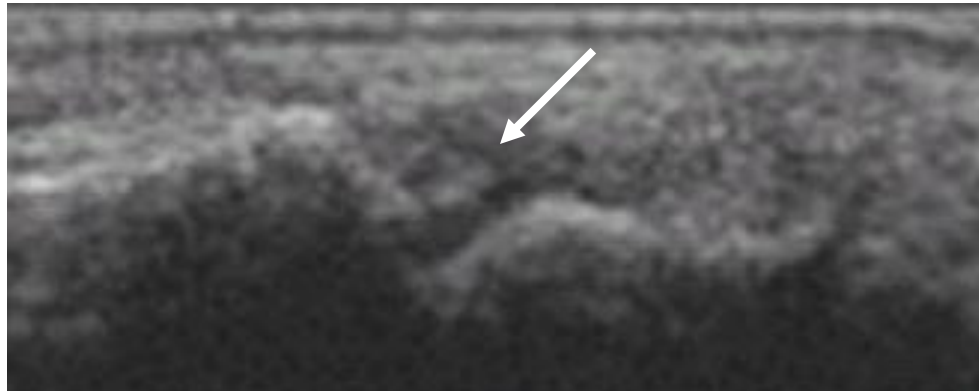


# Dynamics of a cellular infiltrate





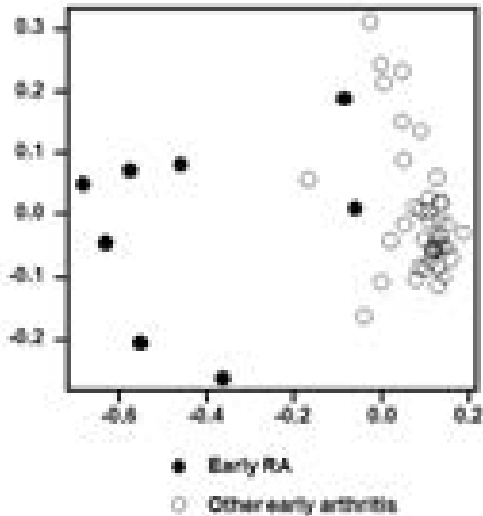
# Synovial pathology in early arthritis







# Synovial fluid cytokine and growth factor profiles in very early RA...



## T cell related

IL-2  
IL-4  
IL-13  
IL-17

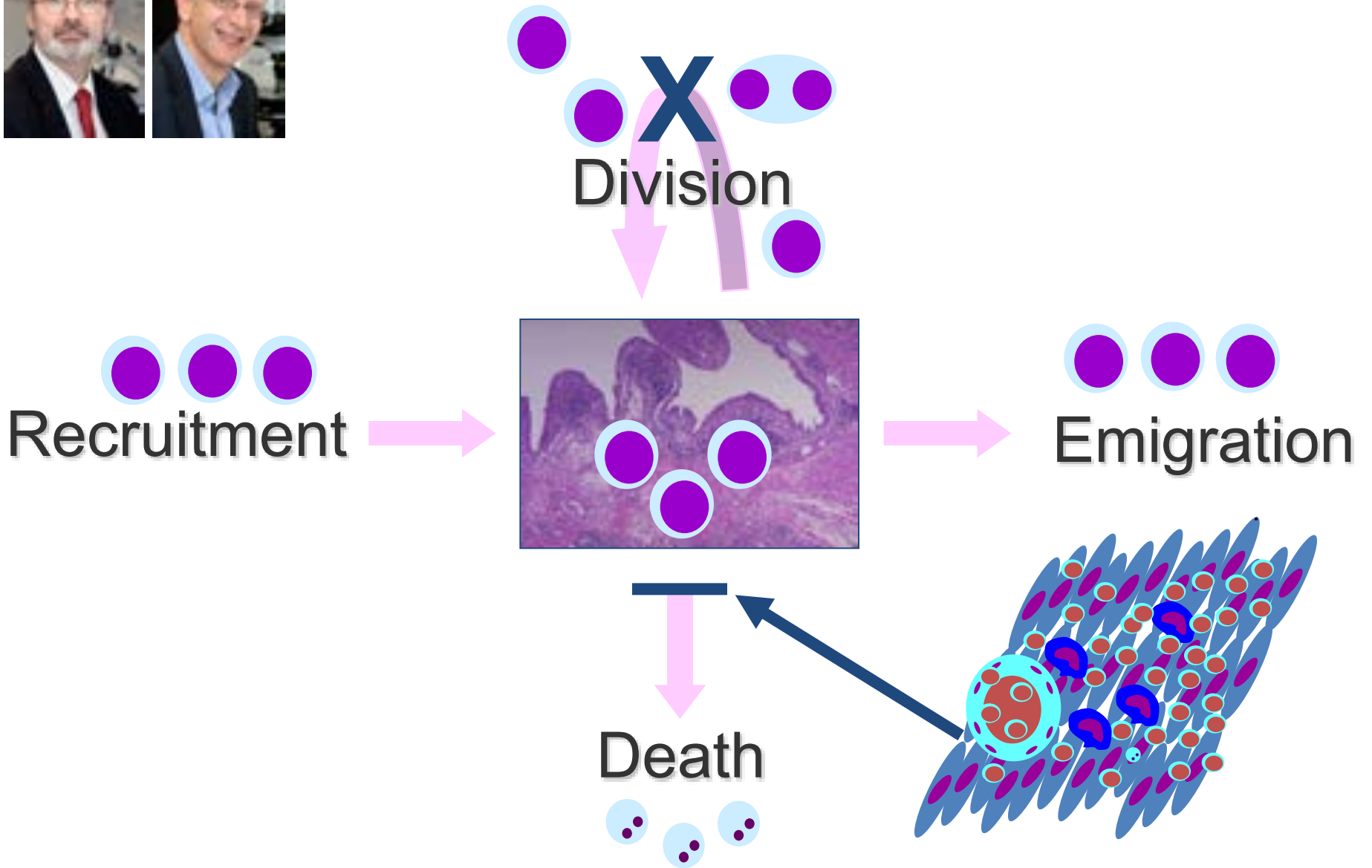
## Anti-apoptotic

IL-15  
GM-CSF  
VEGF

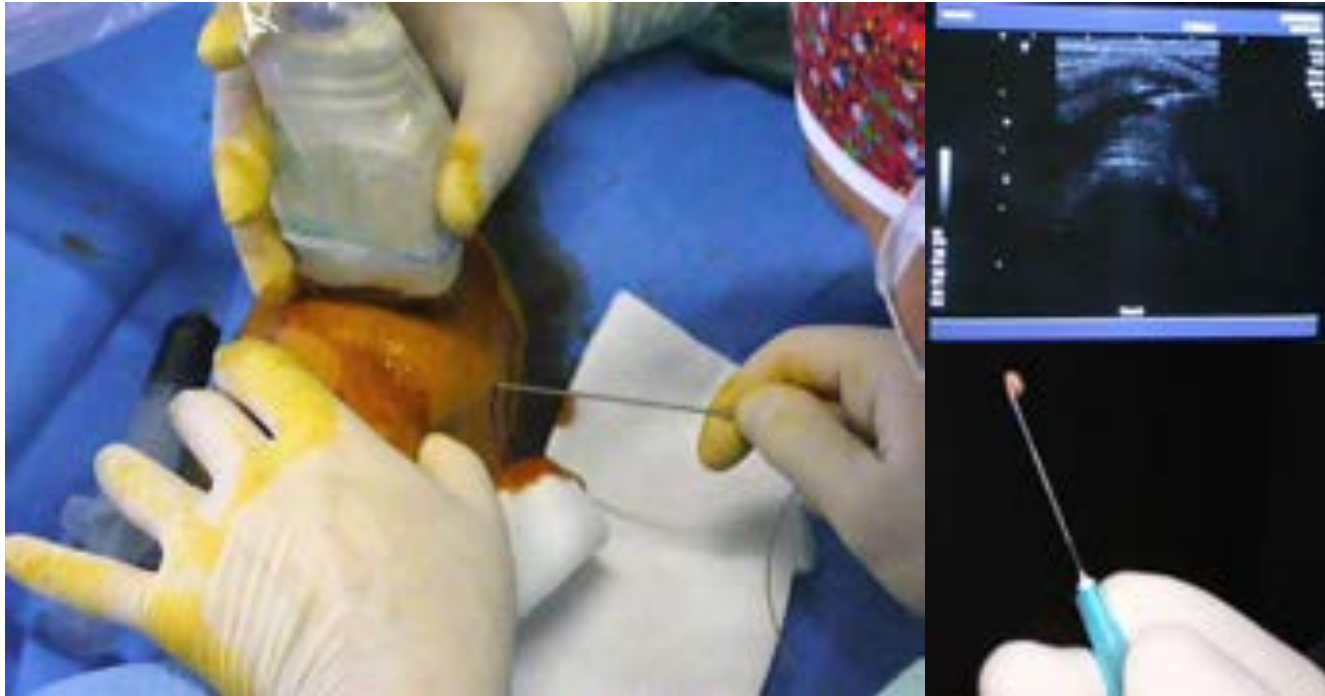
## Stromal

bFGF  
EGF

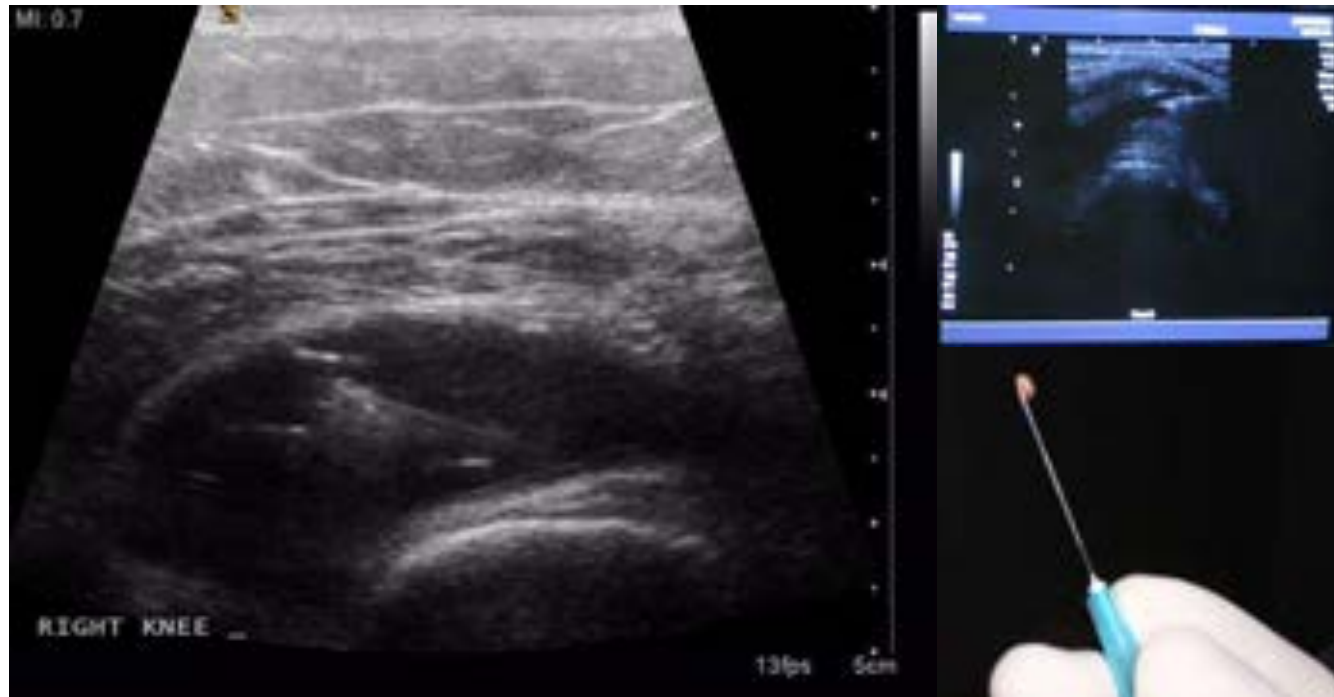




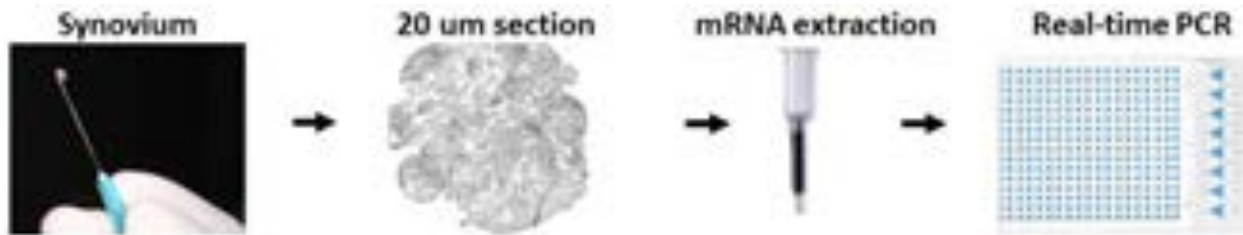
# Ultrasound guided synovial biopsy



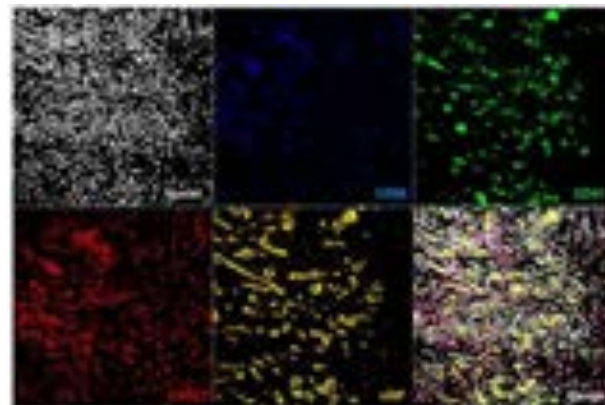
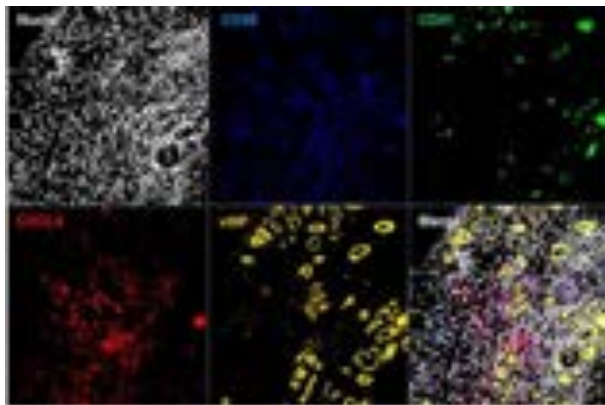
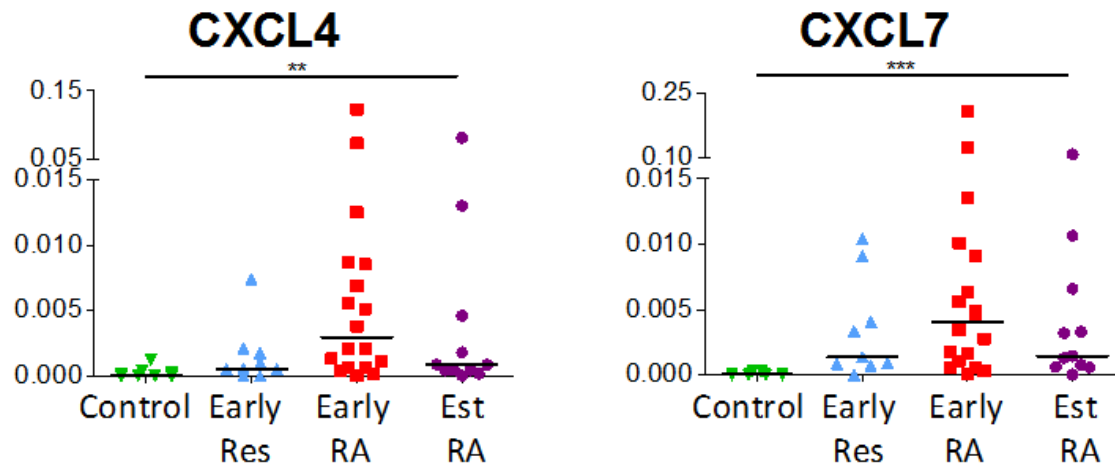
# Ultrasound guided synovial biopsy

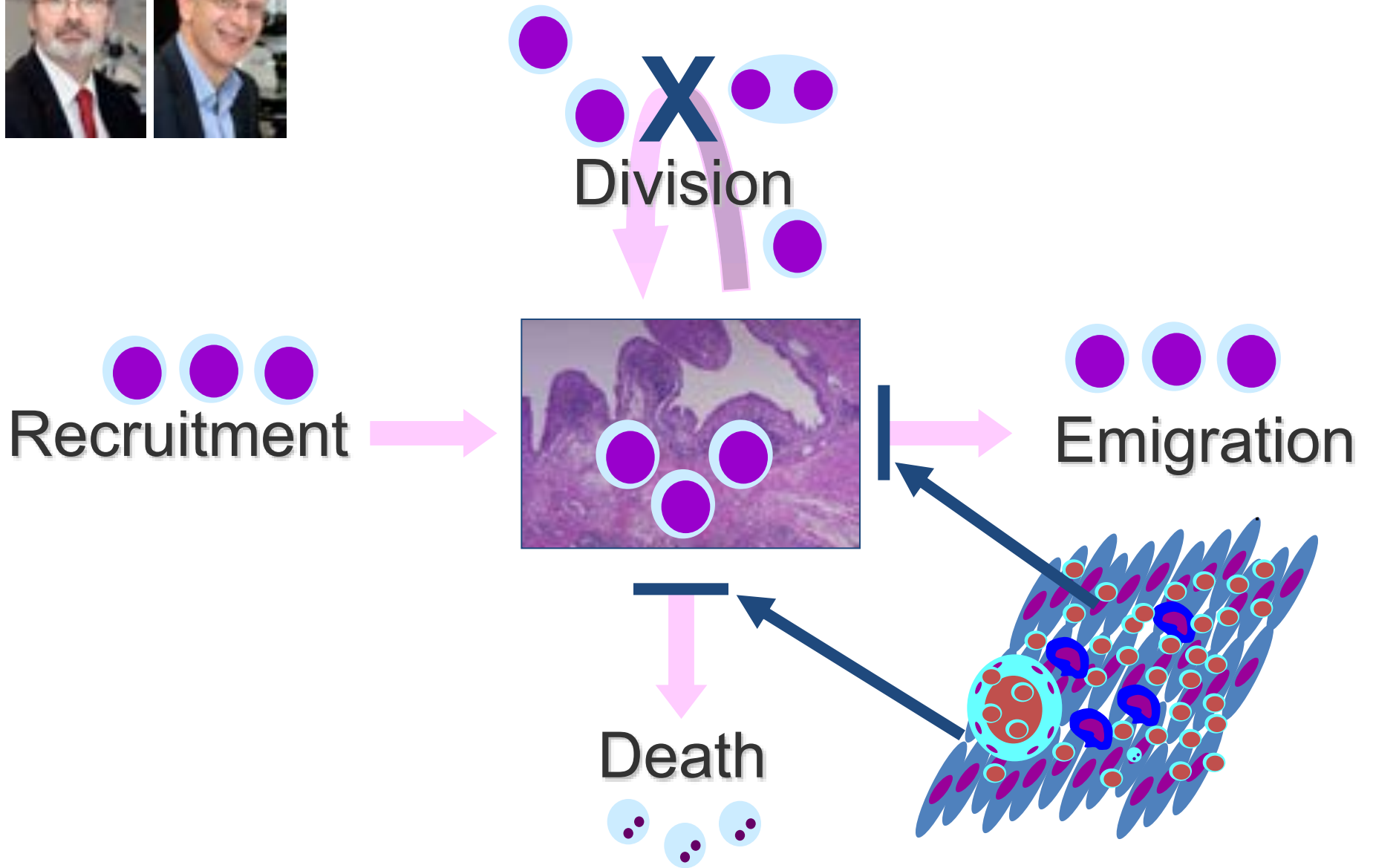


# Synovial tissue cytokine expression

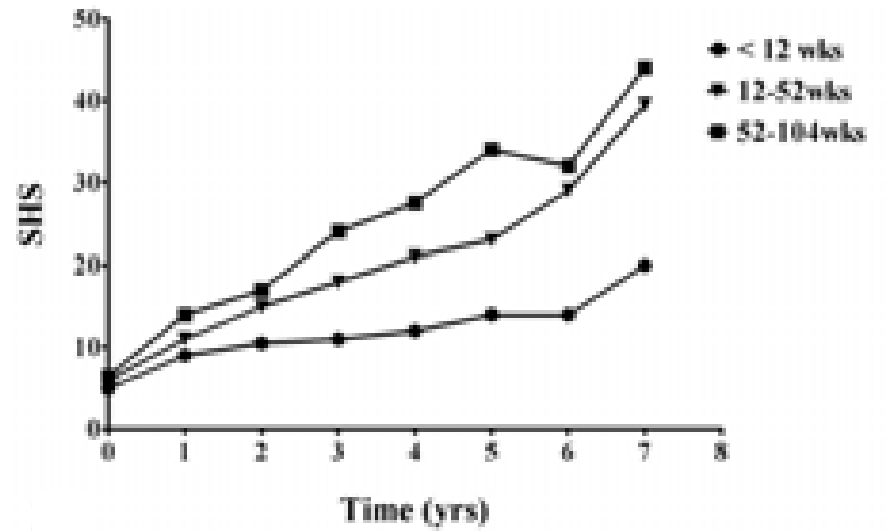
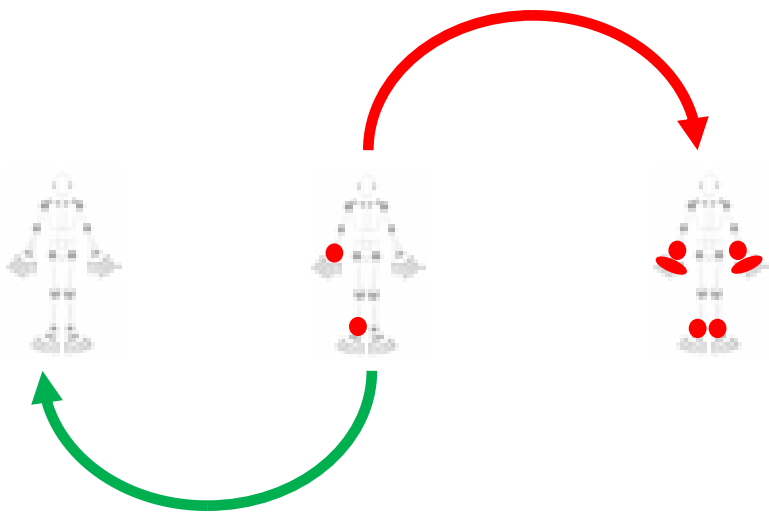


# CXCL4 and CXCL7 mRNA expression in early arthritis









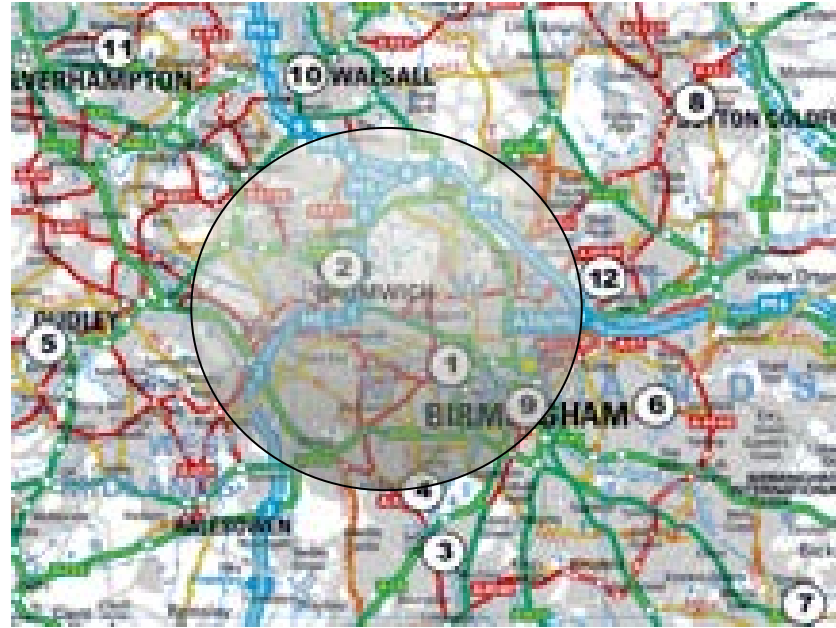
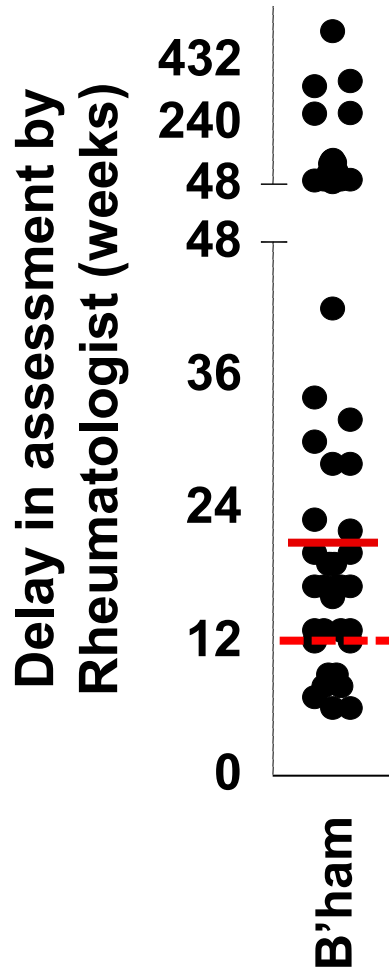
## Early Arthritis Clinics: If You Build It Will They Come?



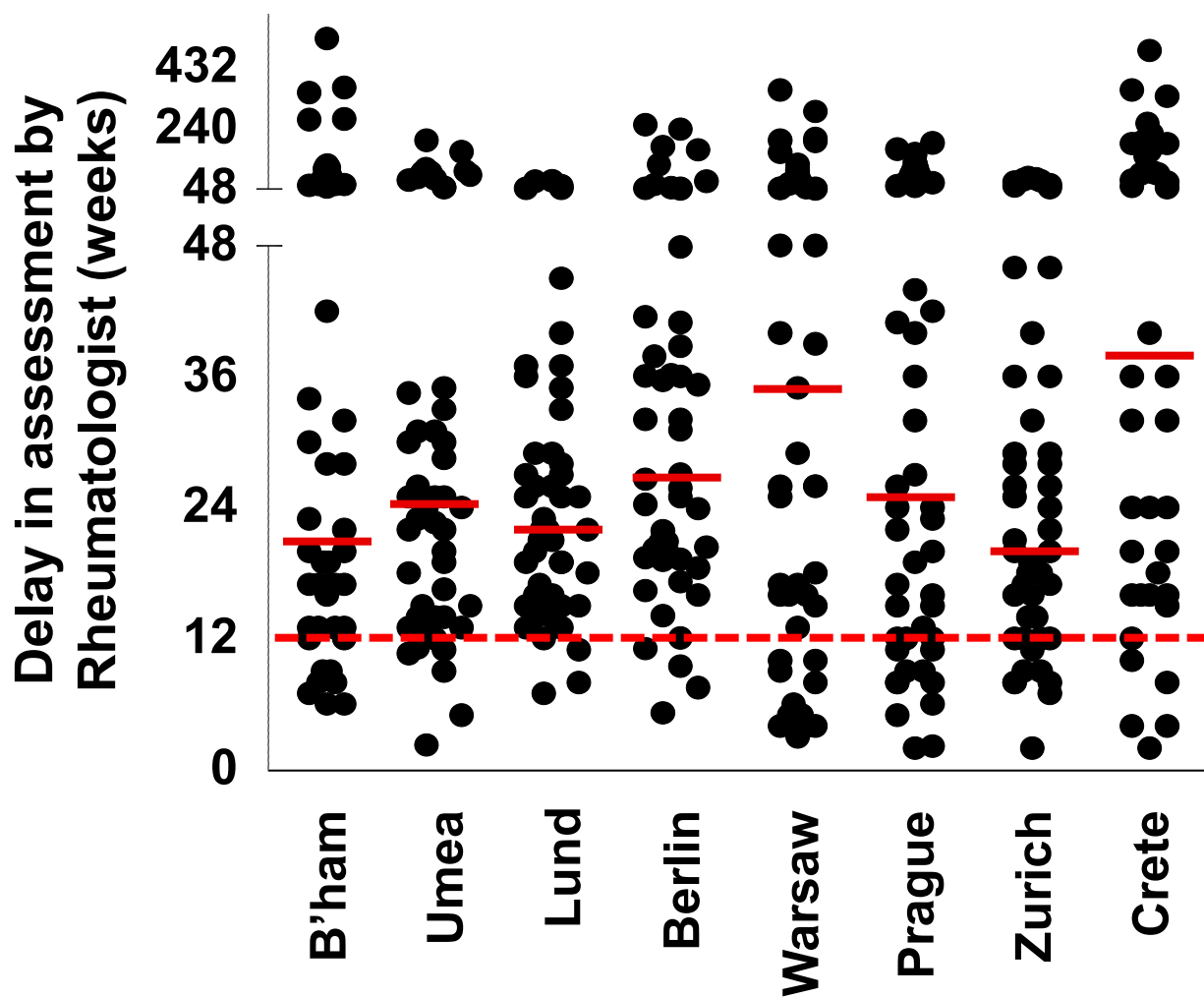
In this issue of *The Journal*, Raza and coworkers examine the utility of anti-cyclic citrullinated peptide (CCP) antibodies in patients with very early inflammatory arthritis<sup>7</sup>. Their findings clearly show the practicality and importance of serologic testing for both serum rheumatoid factor (RF) and anti-CCP antibodies in making an accurate diagnosis in those with persistent symptoms of RA. These findings serve as a challenge to the rheumatologist to amend the manner in which early arthritis patients are currently diagnosed and treated.



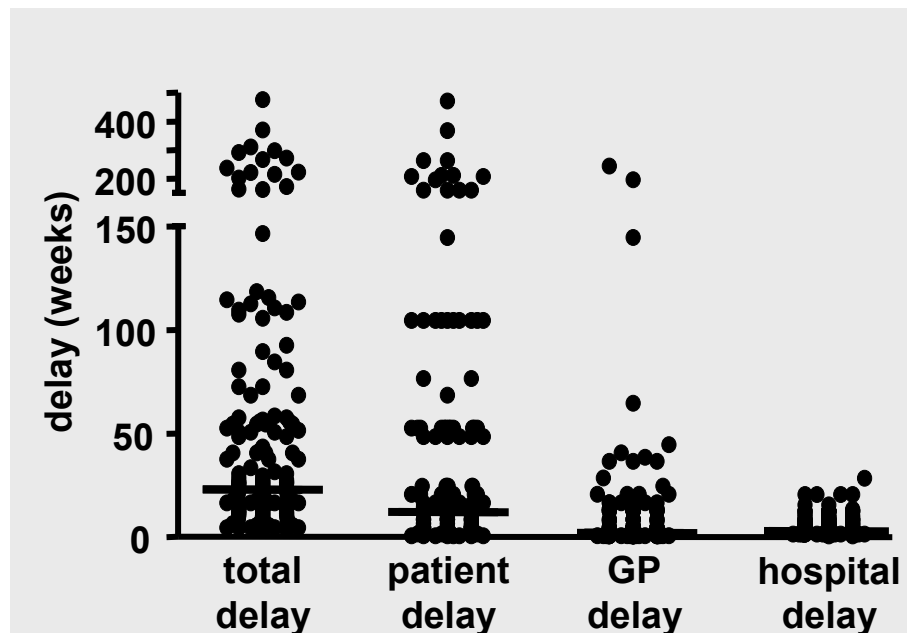
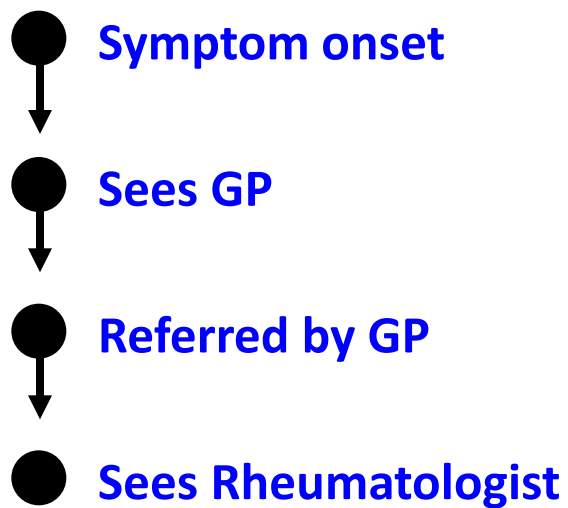
# Capturing patients early: how well do we do?



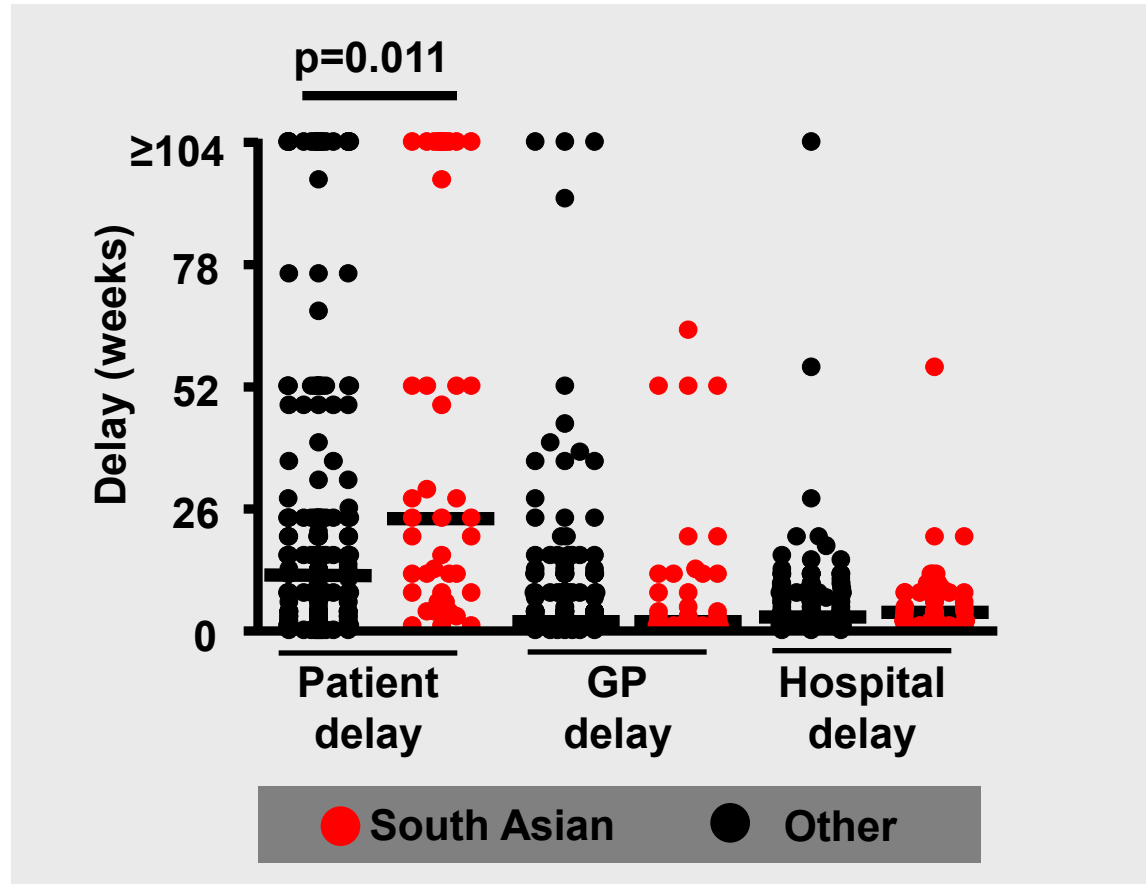
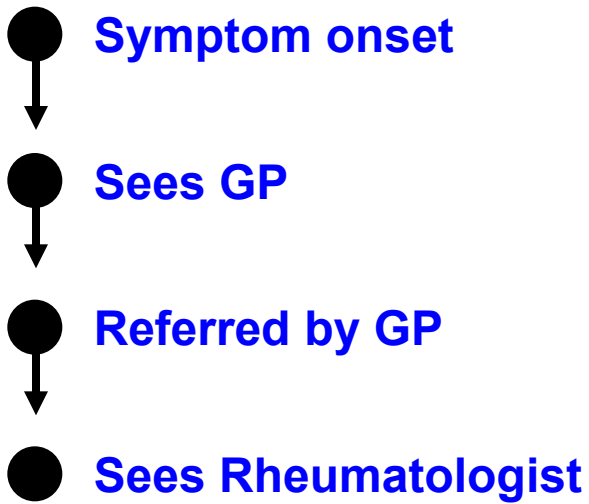
# Capturing patients early: how well do we do?



# Delays in assessment



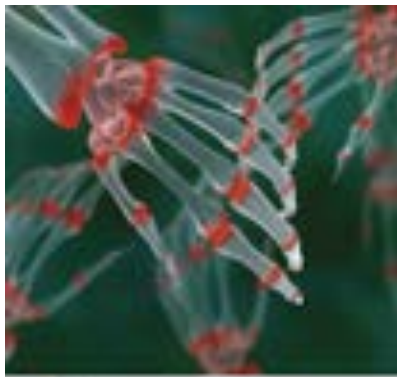
# Delays in assessment in Birmingham: influence of ethnicity



# Four main themes explained patient delays

- **Symptom experience:** an insidious onset of mild symptoms.
- **Symptom evaluation:** an attribution of symptoms to specific inducing factors (e.g. exercise / lack of exercise).
- **Lack of knowledge of RA and available therapies**
- **Negative experience of and attitudes towards health care providers**





Services for people with rheumatoid arthritis

[www.nhs.uk/healthcareprofessionals/rheumatoidarthritis](http://www.nhs.uk/healthcareprofessionals/rheumatoidarthritis)

7 Productivity gains could be achieved and patient quality of life improved through better integration and coordination of services, leading to quicker diagnosis and earlier treatment, but in the short-term costs to the NHS would increase. Currently, ten per cent of people with the disease are treated within three months of symptom onset. Our economic modelling suggests increasing this to 20 per cent could initially increase costs to the NHS by £11 million over five years due to higher expenditure on drugs and the associated costs of monitoring people with the disease (after around nine years, earlier treatment could become cost neutral to the NHS). This increase in earlier treatment could, however, result in productivity gains of £31 million for the economy due to reduced sick leave and lost employment.

UNIVERSITY OF BIRMINGHAM

Birmingham Rheumatology Research Patient Partnership (R2P2)

**R2P2 News**

- 18th November 2015
- 17th November 2015
- 16th November 2015

**What is R2P2?**

Rheumatoid arthritis (RA) is a chronic inflammatory disease that affects the joints. It is a complex condition and the exact cause is unknown. The Birmingham Rheumatology Research Patient Partnership (R2P2) is a group of people with RA who are working with researchers at the University of Birmingham to improve the understanding of RA and to develop new treatments. R2P2 is a partnership between patients and researchers.

**What is Rheumatoid Arthritis (RA)?**

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**Membership - Research Group (R2P2)**

**Current Research Projects**

Swollen joints  
Stiffness  
Pain

BETTER TO BE CLEAR

