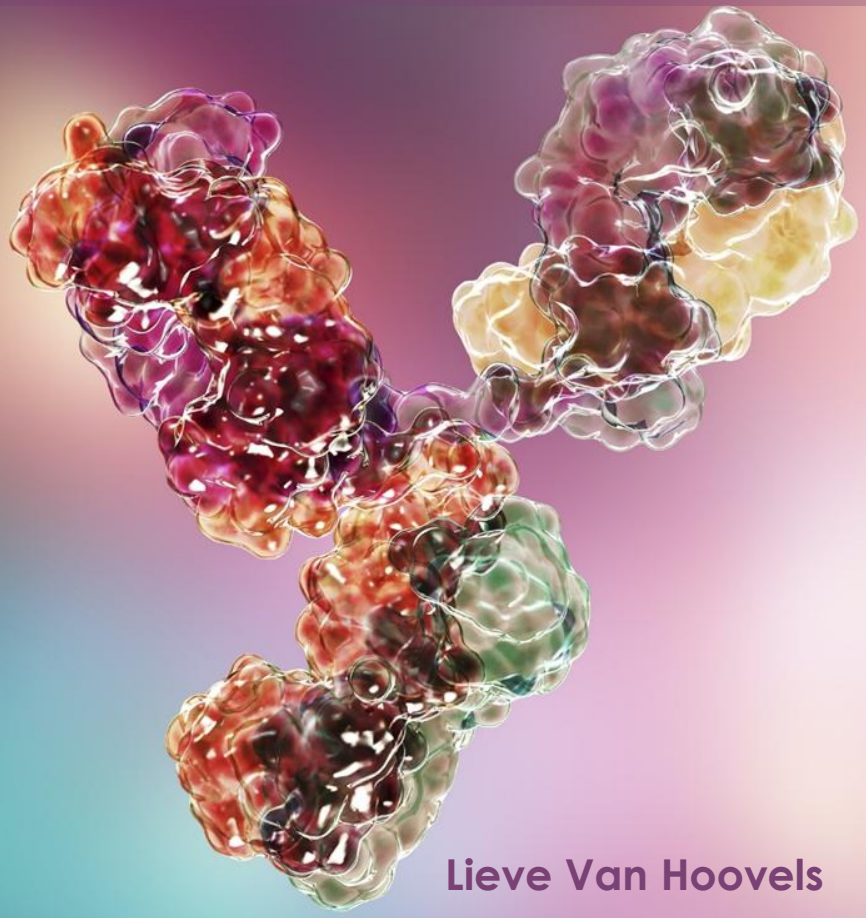
It is time to revise RA classification by changing RF and ACPA scores



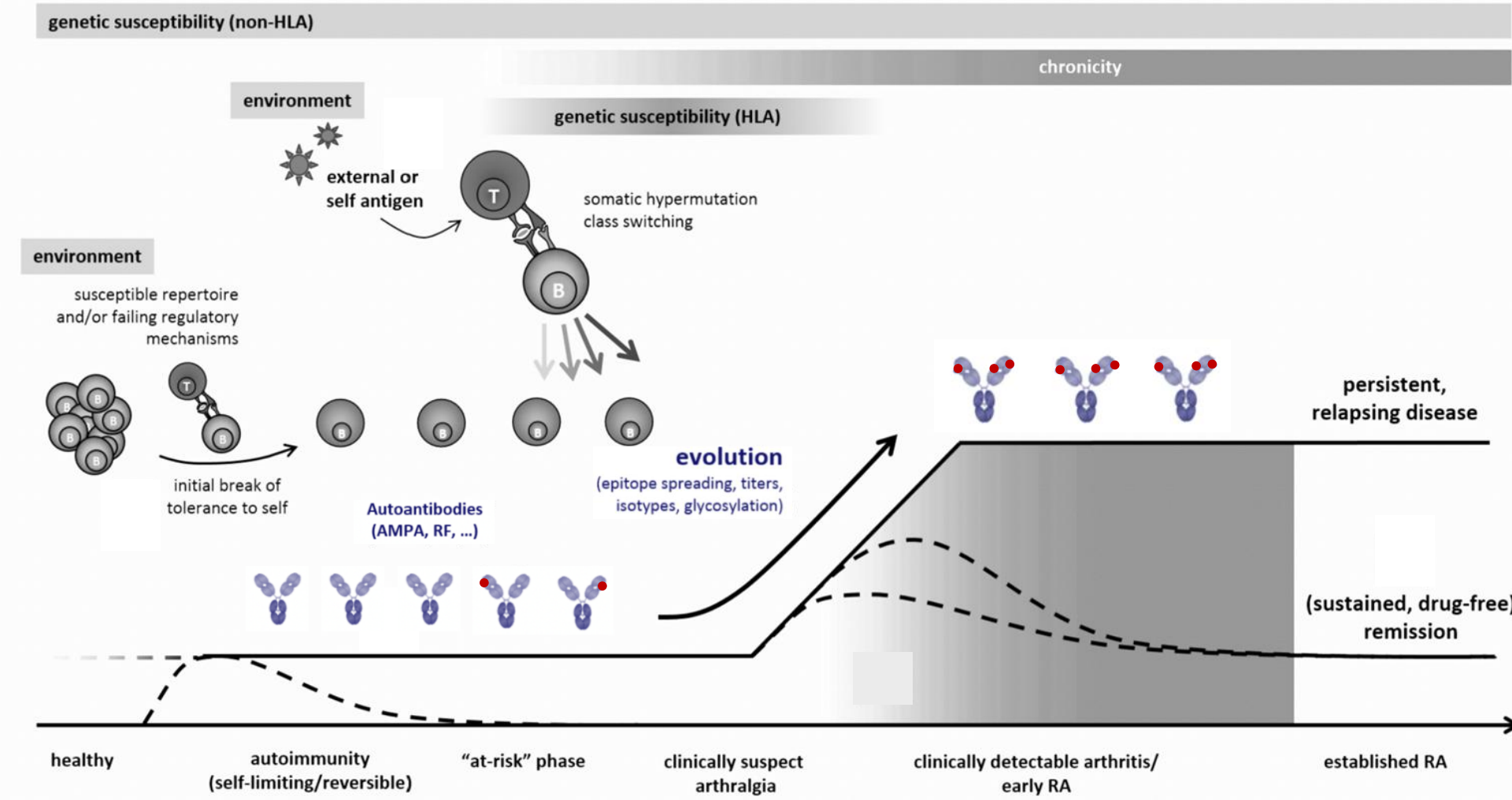
Lieve Van Hoovels

12th International Autoimmunity Seminar, Werfen
Oct 15th, 2025

KU LEUVEN

AZORO

1. RF/ACPA testing in RA

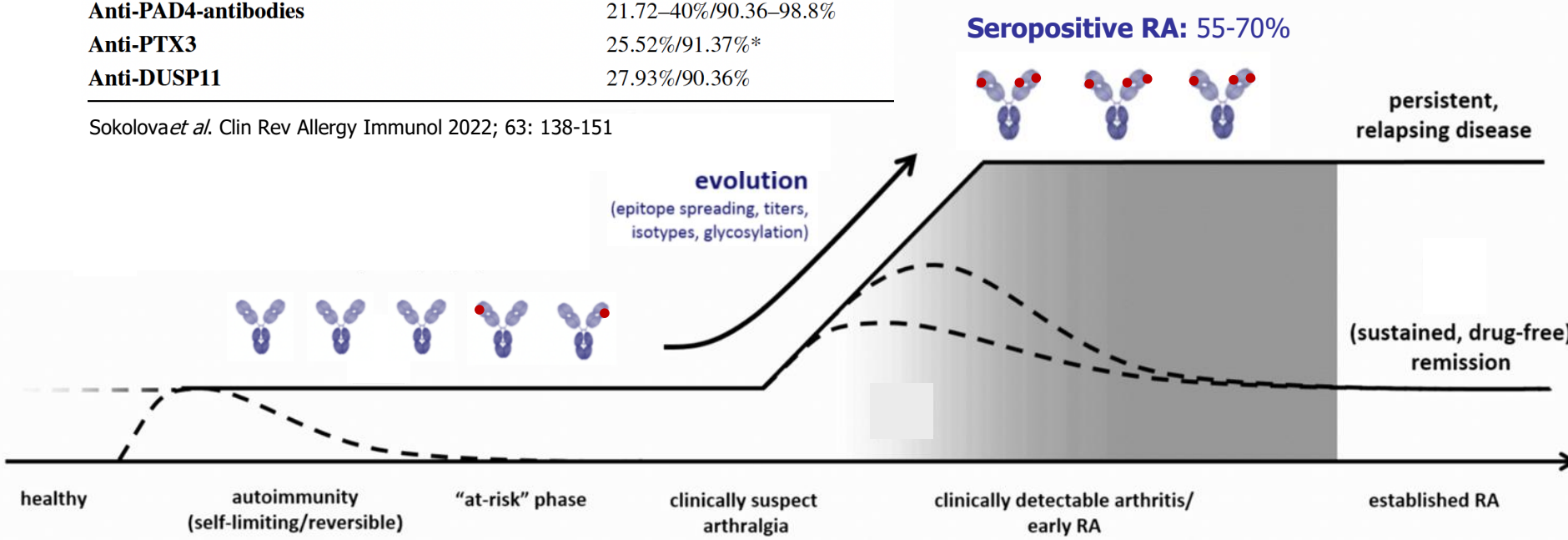


Scherer *et al*. J Autoimmun 2020; 110: 102400

1. RF/ACPA testing in RA

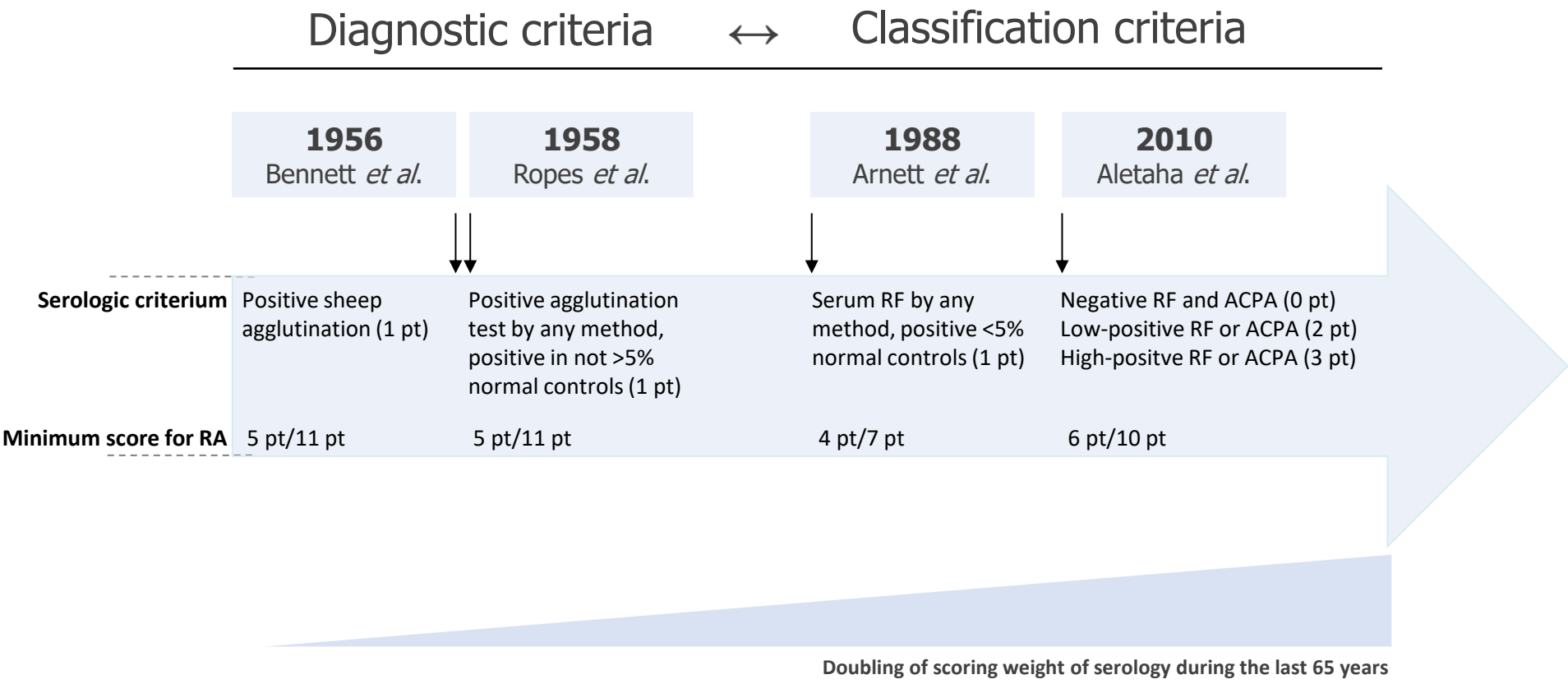
Autoantibody	Sensitivity/specificity
RF	60–90%/85%
ACPA (CCP2)	41–74.8%/91–100%
ACPA (CCP3)	77.5–78.8%/87.8–96.6%
ACPA (CCP3.1)	74–83%/89.6–98.3%
Anti-CarP (*carbamylated fetal calf serum)	35–46.8%/91.95–92.8%
Anti-acetylated vimentin antibodies	36.6%/86.2%
Anti-PAD4-antibodies	21.72–40%/90.36–98.8%
Anti-PTX3	25.52%/91.37%*
Anti-DUSP11	27.93%/90.36%

Sokolova*et al.* Clin Rev Allergy Immunol 2022; 63: 138-151



Scherer*et al.* J Autoimmun 2020; 110: 102400

1. RF/ACPA testing in RA



Bennett *et al*. Bull Rheum Dis 1956; 7: 121-4
Ropes *et al*. Bull Rheum Dis 1958; 9: 175-6
Arnett *et al*. Arthritis Rheum 1988; 31: 315-24
Aletaha *et al*. ARD 2010; 69: 1580-8
Van Hoovels *et al*. J Transl Autoimmun 2022; 5: 100142

1. RF/ACPA testing in RA

ACR 1987

1. Morning stiffness
2. Arthritis of 3 or more joint areas
3. Arthritis of hand joints
4. Symmetric arthritis
5. Rheumatoid nodules
6. Serum rheumatoid factor
7. Radiographic changes

≥ 4/7=RA

ACR/EULAR 2010

Classification criteria for RA (score-based algorithm: add score of categories A–D; a score of ≥6/10 is needed for classification of a patient as having definite RA)‡

A. Joint involvement§	
1 large joint¶	0
2–10 large joints	1
1–3 small joints (with or without involvement of large joints)#	2
4–10 small joints (with or without involvement of large joints)	3
>10 joints (at least 1 small joint)**	5
B. Serology (at least 1 test result is needed for classification)††	
Negative RF *and* negative ACPA	0
Low-positive RF *or* low-positive ACPA	2
High-positive RF *or* high-positive ACPA	3
C. Acute-phase reactants (at least 1 test result is needed for classification)‡‡	
Normal CRP *and* normal ESR	0
Abnormal CRP *or* abnormal ESR	1
D. Duration of symptoms§§	
<6 weeks	0
≥6 weeks	1

≥ 6/10=RA

Arnett *et al.* Arthritis Rheum 1988; 31: 315-24
Aletaha *et al.* ARD 2010; 69: 1580-8

1. RF/ACPA testing in RA

ACR 1987

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5. Rheumatoid nodules
6. Serum rheumatoid factor
7. Radiographic changes

ACR/EULAR 2010

Classification criteria for RA (score-based algorithm: add score of categories A–D; a score of ≥6/10 is needed for classification of a patient as having definite RA)‡

A. Joint involvement§
   - 1 large joint¶ 0
   - 2–10 large joints 1
   - 1–3 small joints (with or without involvement of large joints)# 2
   - 4–10 small joints (with or without involvement of large joints) 3

B. Serology (at least 1 test result is needed for classification)††

Negative RF *and* negative ACPA	**≤ ULN**	0
Low-positive RF *or* low-positive ACPA	**> ULN but ≤ 3x ULN**	2
High-positive RF *or* high-positive ACPA	**> 3x ULN**	3

C. Acute-phase reactants (at least 1 test result is needed for classification)‡‡
   - Normal CRP *and* normal ESR 0
   - Abnormal CRP *or* abnormal ESR 1

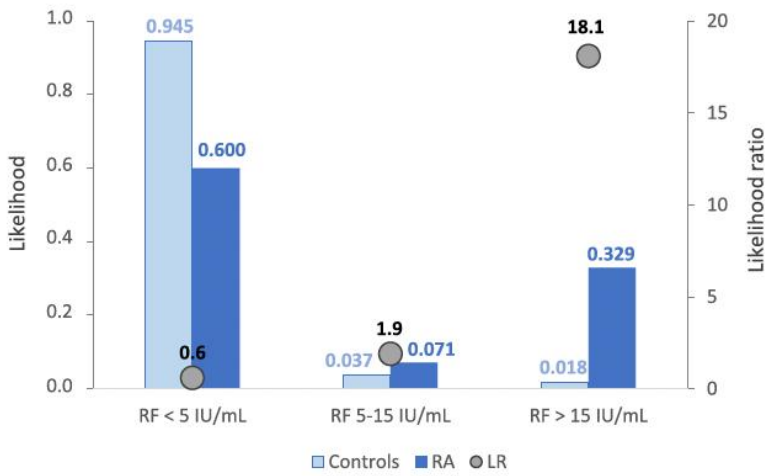
D. Duration of symptoms§§
   - <6 weeks 0
   - ≥6 weeks 1

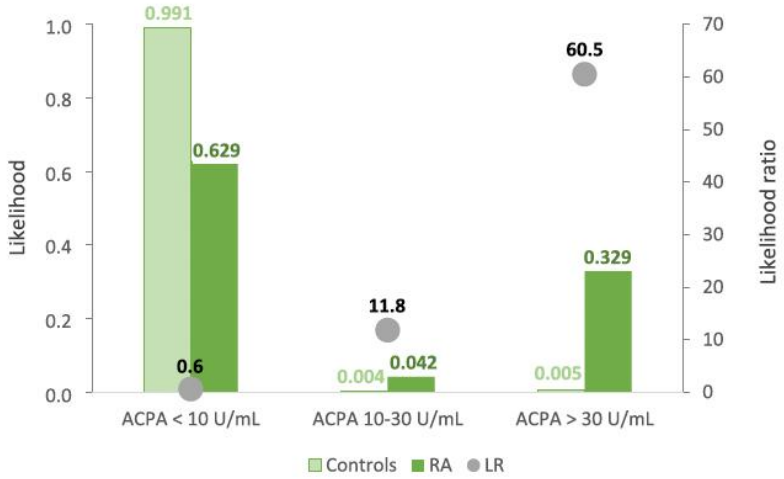
≥ 6/10=RA

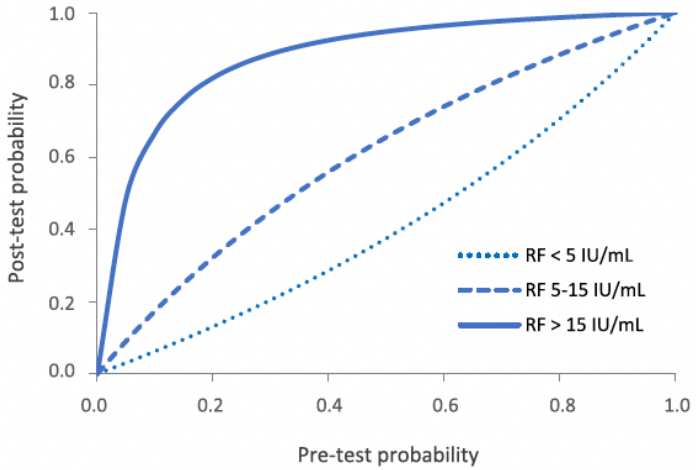
Aletaha *et al*. ARD 2010; 69: 1580-8

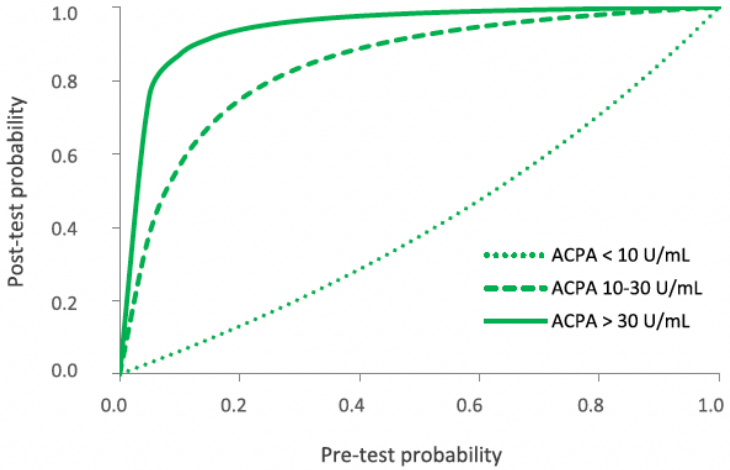
1. RF/ACPA testing in RA

Likelihood ratio









Van Hoovels *et al.* J Transl Autoimmun 2022; 5: 100142
Steiner *et al.* RMD Open 2024; 10: e003851

1. RF/ACPA testing in RA

2010 ACR/EULAR vs 1987 ACR RA classification criteria

↑ Sensitivity = 73.5-84%

↓ Specificity = 60-71%

van der Linden *et al*. Arthritis Rheum 2011: 63; 37-42
Kaneko *et al*. Rheumatology 2011: 50; 1268-74
Cader *et al*. ARD 2011; 70: 949-50
Alves *et al*. ARD 2011; 70; 1645-7

Category	Misclassified	
	False positive n=44	False negative n=22
Joint involvement		
1 large joint (%)	0 (0)	0 (0)
2–10 large joints (%)	0 (0)	2 (9.1)
1–3 small joint (%)	1 (2.3)	7 (31.8)
4–10 small joints (%)	3 (6.8)	10 (45.5)
>10 joints (%)	40 (90.9)	3 (13.6)
Serology		
Normal RF or ACPA (%)	35 (79.6)	18 (81.8)
Low positive RF or ACPA (%)	1 (2.3)	1 (4.6)
High positive RF or ACPA	8 (18.2)	3 (13.6)
Acute-phase reactants		
Normal CRP or ESR (%)	14 (31.8)	9 (40.9)
Abnormal CRP or ESR (%)	30 (68.2)	13 (59.1)
Symptoms duration		
<6 weeks	14 (31.8)	10 (45.5)
≥6 weeks	30 (68.2)	12 (54.6)
Score, median (IQR)	7 (6;7)	5 (5;5.75)

Biliavska *et al*. ARD 2013; 72: 1335-1341

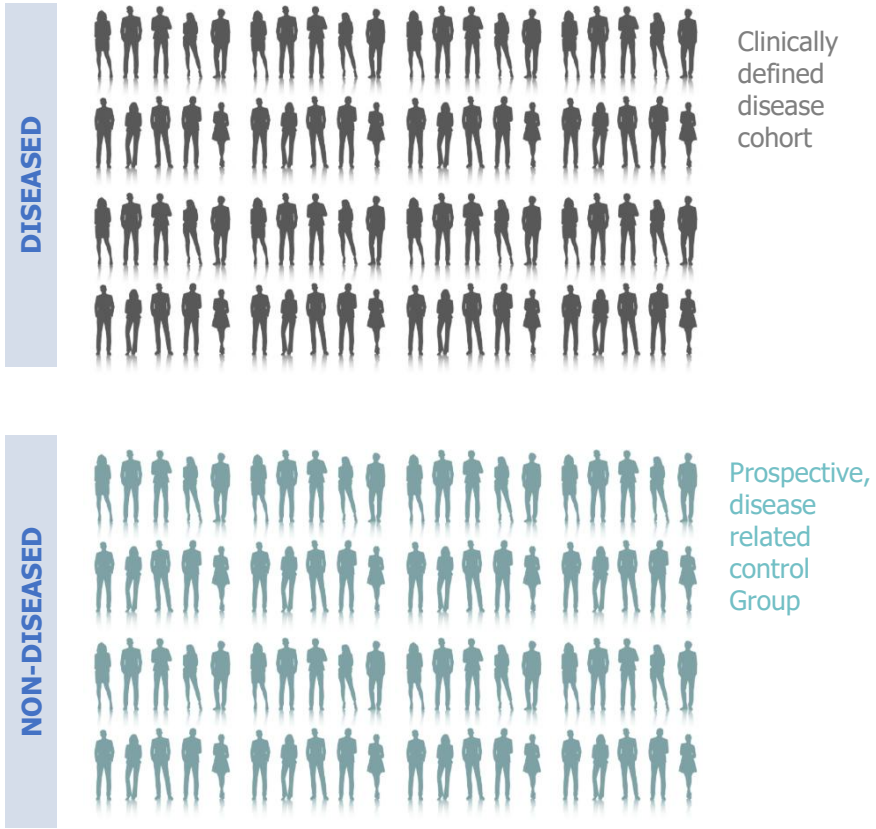
Impact of serology

Refining the contribution of serological measures in RA classification

Steiner *et al*. Autoimmun Rev 2023: 103421

2.1 Materials and Methods

Investigative cohort



Demographics

European, multicenter (n=11) cohort

RA (n=398)
F=68.6%; median age= 57 [18-86]

Non-RA diseased control cohort (n=448)
F=74.8%; median age= 53 [11-92]

Methods

RF/ACPA serology of:
- Thermo Fisher
- Orgentec
- Roche
- Abbott
- Siemens

Data analysis

RA LR based on manufacturer's cut-off RF/ACPA
RA classification:
- Impact of RF/ACPA serology
- Optimalization RF/ACPA scoring weight

Van Hoovels *et al.* RMD Open 2022; e002099

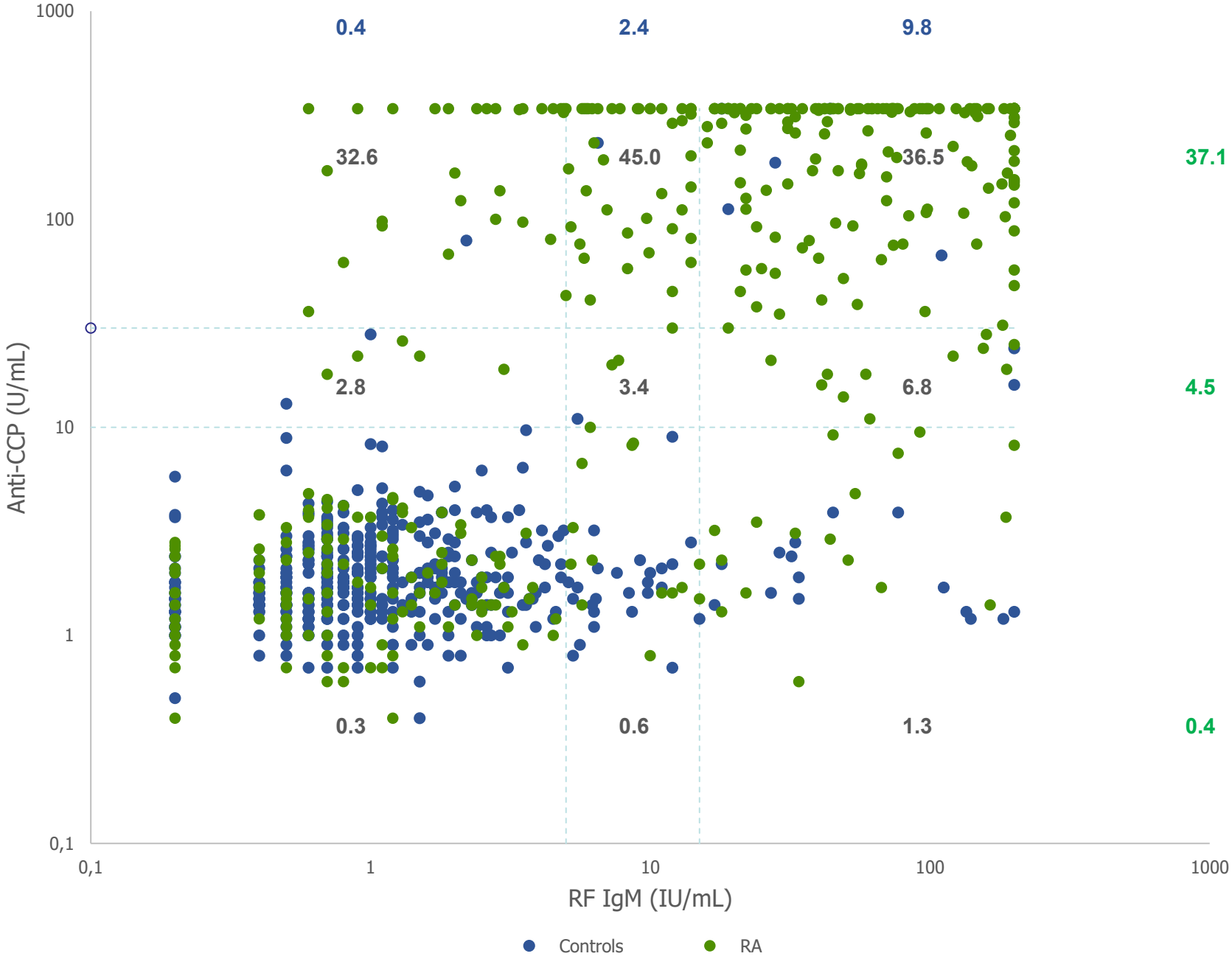
3.1 Test result interval-specific LRs

Investigative cohort

	Thermo Fisher	Orgentec	Roche	Abbott	Siemens
RF neg	0.42 (0.37-0.48)	0.52 (0.47-0.58)	0.40 (0.35-0.46)	0.51 (0.46-0.56)	0.37 (0.32-0.44)
RF low	2.4 (1.5-3.6)	2.5 (1.7-3.8)	2.5 (1.7-3.7)	8.7 (4.7-16.1)	2.4 (1.7-3.5)
RF high	9.8 (6.4-14.9)	17.8 (9.2-34.4)	14.2 (8.4-24.1)	13.6 (7.3-25.6)	11.2 (6.9-18.6)
ACPA neg	0.37 (0.33-0.43)	0.43 (0.38-0.48)	0.39 (0.34-0.44)	0.38 (0.34-0.44)	0.38 (0.33-0.44)
ACPA low	4.5 (1.7-11.9)	16.3 (3.9-68.0)	1.1 (0.45-2.8)	14.6 (3.5-61.3)	2.2 (0.91-5.5)
ACPA high	37.1 (17.7-77.8)	32.5 (15.5-68.2)	33.8 (16.9-67.4)	24.9 (13.4-46.2)	30.0 (15.2-60.8)

LIKELIHOOD FOR RA

LIKELIHOOD FOR RA


1000
100
10
1
0,1
Anti-CCP (U/mL)
0,1
1
10
100
1000
RF IgM (IU/mL)
0.4
2.4
9.8
32.6
45.0
36.5
37.1
2.8
3.4
6.8
4.5
0.3
0.6
1.3
0.4
Controls
RA

3.1 Test result interval-specific LRs

Investigative cohort

LIKELIHOOD FOR RA

	Thermo Fisher	Orgentec	Roche	Abbott	Siemens
ACPA neg RF neg	0.33 (0.28-0.39)	0.39 (0.34-0.45)	0.33 (0.29-0.39)	0.33 (0.29-0.39)	0.31 (0.26-0.37)
ACPA neg RF low	0.63 (0.33-1.20)	0.48 (0.24-0.95)	0.67 (0.38-1.19)	3.2 (1.4-7.5)	0.77 (0.47-1.3)
ACPA neg RF high	1.3 (0.65-2.5)	2.4 (0.99-5.9)	1.4 (0.68-2.84)	0.84 (0.30-2.4)	1.4 (0.67-3.0)
ACPA low RF neg	2.8 (0.55-14.4)	9.0 (1.1-71.7)	0.38 (0.10-1.38)	5.6 (1.2-25.5)	1.4 (0.38-5.2)
ACPA low RF low	3.4 (0.35-32.3)	6.8 (0.82-55.9)	Infinite[a] n.a.	Infinite[a] n.a.	0.56 (0.05-6.2)
ACPA low RF high	6.8 (1.5-30.0)	Infinite[a] n.a.	Infinite[a] n.a.	Infinite[a] n.a.	8.9 (1.1-71.7)
ACPA high RF neg	32.6 (4.5-238.5)	15.8 (4.9-50.4)	13.5 (3.2-56.8)	16.0 (5.9-43.8)	17.8 (2.4-135.2)
ACPA high RF low	45.0 (6.2-326.0)	27.0 (6.6-110.4)	13.7 (5.6-33.8)	16.0 (5.9-43.8)	17.2 (6.4-47.5)
ACPA high RF high	36.5 (15.1-87.9)	63.0 (15.7-253.5)	174.5 (24.5-1240.7)	60.2 (15.0-242.3)	51.1 (16.3-161.2)

[a]This serological combination was not revealed in any of the control patients

3.2 Impact of serology on RA classification

ACR/EULAR 2010 RA classification

	RA	Non-RA
	% ≥ 6	% ≥ 6
Clinical score	23.9	5.1
Including inflammation	26.9	5.4
Including RF Assays	**ACR/EULAR 2010**	**ACR/EULAR 2010**
Thermo Fisher RF IgM	64.6	10.5
Roche RF	65.1	8.9
Orgentec RF IgM	58.3	7.8
Abbott RF	57.5	7.4
Siemens RF	67.4	10.2
Range	**57.5-67.4%**	**7.4-10.5%**
Including ACPA assays	**ACR/EULAR 2010**	**ACR/EULAR 2010**
Thermo Fisher ACPA	66.1	6.3
Roche ACPA	66.3	6.5
Orgentec ACPA	62.6	6.3
Abbott ACPA	65.6	6.3
Siemens ACPA	66.9	6.2
Range	**62.6-66.9%**	**6.2-6.5%**
Including RF/ACPA assays	**ACR/EULAR 2010**	**ACR/EULAR 2010**
Thermo Fisher RF IgM/ACPA	72.1	10.5
Roche RF/ACPA	71.9	9.8
Orgentec RF IgM/ACPA	67.8	8.5
Abbott RF/ACPA	70.1	7.8
Siemens RF/ACPA	74.0	10.2
Range	**67.8-74.0%**	**7.8-10.5%**

Δ in RA misclassification mainly due to RF

Van Hoovels *et al.* ARD 2018; 77: 667-77
Falkenburg *et al.* CCLM 2018; 16: 1749-1758

3.2 Impact of serology on RA classification

Optimalization RF/ACPA scoring weights

Assignment Array	Manufacturer	Sensitivity	1 - Specificity
	Thermofisher	0,268844221	0,053571429
	Abbot	0,268844221	0,053571429
[[0, 0, 0], [0, 0, 0], [0, 0, 0]]	Roche	0,268844221	0,053571429
	Orgentec	0,268844221	0,053571429
	Siemens	0,281767956	0,054726368
	Thermofisher	0,371859296	0,055803571
	Abbot	0,341708543	0,053571429
[[0, 0, 0], [0, 0, 0], [0, 0, 1]]	Roche	0,371859296	0,053571429
	Orgentec	0,349246231	0,053571429
	Siemens	0,38121547	0,054726368
	Thermofisher	0,484924623	0,055803571
	Abbot	0,424623116	0,053571429
[[0, 0, 0], [0, 0, 0], [0, 0, 2]]	Roche	0,479899497	0,053571429
	Orgentec	0,424623116	0,055803571
	Siemens	0,486187845	0,054726368
	Thermofisher	0,527638191	0,058035714
	Abbot	0,449748744	0,053571429
[[0, 0, 0], [0, 0, 0], [0, 0, 3]]	Roche	0,522613065	0,053571429
	Orgentec	0,452261307	0,055803571
	Siemens	0,516574586	0,05721393
	Thermofisher	0,547738693	0,060267857
	Abbot	0,457286432	0,055803571
[[0, 0, 0], [0, 0, 0], [0, 0, 4]]	Roche	0,542713568	0,055803571
	Orgentec	0,459798995	0,058035714
	Siemens	0,538674033	0,059701493
	Thermofisher	0,557788945	0,0625
	Abbot	0,459798995	0,055803571
[[0, 0, 0], [0, 0, 0], [0, 0, 5]]	Roche	0,550251256	0,055803571
	Orgentec	0,469849246	0,058035714
	Siemens	0,546961326	0,059701493
	Thermofisher	0,291457286	0,053571429
	Abbot	0,301507538	0,058035714
[[0, 0, 0], [0, 0, 0], [0, 1, 0]]	Roche	0,306532663	0,055803571
	Orgentec	0,296482412	0,053571429
	Siemens	0,32320442	0,05721393
	Thermofisher	0,394472362	0,055803571
	Abbot	0,374371859	0,058035714
[[0, 0, 0], [0, 0, 0], [0, 1, 1]]	Roche	0,409547739	0,055803571
	Orgentec	0,376884422	0,053571429
	Siemens	0,422651934	0,05721393
	Thermofisher	0,507537688	0,055803571
	Abbot	0,457286432	0,058035714
[[0, 0, 0], [0, 0, 0], [0, 1, 2]]	Roche	0,51758794	0,055803571
	Orgentec	0,452261307	0,055803571
	Siemens	0,527624309	0,05721393

...

- **Error grid** analysis accross all integer RF/ACPA scores (scikit-learn library, Python)
- >23000 possible combinations
- In line with RA LR results of RF/ACPA serology
- **Highest specificity** in RA classification:

ACPA	**RF**		
	Negative	**Low positive**	**High positive**
Negative	0	0	1
Low positive	1	3	4
High positive	3	4	5

3.2 Impact of serology on RA classification

RA classification with optimized serological scoring (RCC)

	RA (%)		Non-RA (%)	
	ACR/EULAR 2010	**RCC**	**ACR/EULAR 2010**	**RCC**
	% ≥ 6	**% ≥ 6**	**% ≥ 6**	**% ≥ 6**
Clinical score	23.9	23.9	5.1	5.1
Including inflammation	26.9	26.9	5.4	5.4
Including RF/ACPA assays				
Thermo Fisher RF IgM/ACPA	72.1	73.1	10.5	6.9
Roche RF/ACPA	71.9	72.9	9.8	6.7
Orgentec RF IgM/ACPA	67.8	67.1	8.5	6.5
Abbott RF/ACPA	70.1	68.8	7.8	6.3
Siemens RF/ACPA	74.0	74.0	10.2	6.7
	67.8-74.0	**67.1-74.0**	**7.8-10.5**	**6.3-6.9**

- RCC resulted in decreased RA misclassification of non-RA
- RCC minimally affecting classification sensitivity

3.2 Impact of serology on RA classification

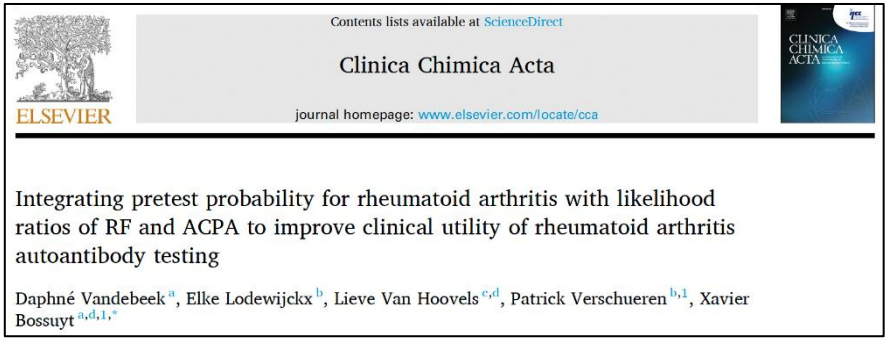
RCC in seropositive patients

	RA (%)		Non-RA (%)	
	ACR/EULAR 2010	RCC	ACR/EULAR 2010	RCC
	% ≥ 6	% ≥ 6	% ≥ 6	% ≥ 6
Clinical score	16.8	16.8	11.5	11.5
Including inflammation	18.8	18.8	11.5	11.5
Including RF/ACPA assays				
Thermo Fisher RF IgM/ACPA	90.4	91.8	55.8	25.0
Roche RF/ACPA	89.4	90.8	38.3	15.0
Orgentec RF IgM/ACPA	89.9	88.7	42.9	21.4
Abbott RF/ACPA	89.0	87.2	51.9	25.9
Siemens RF/ACPA	88.8	88.8	38.3	15.0
	88.8-90.4	**87.2-91.8**	**38.3-55.8**	**15.0-25.9**

- RCC resulted in decreased RA misclassification of non-RA
- RCC did not affect diagnostic sensitivity

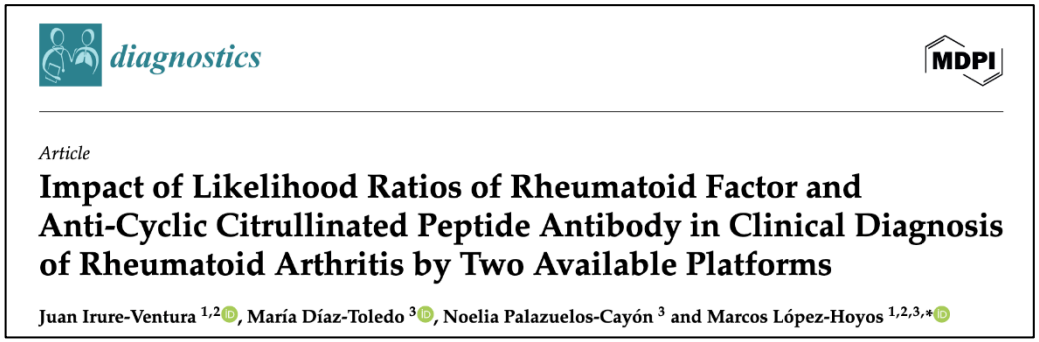
2.2 Materials and Methods

Confirmatory cohorts



RA= 67; Non-RA =441
RF IMMAGE®800 (Beckman Coulter); ACPA EliA IgG (Thermo Fisher)

RA= 132; Non-RA = 193
RF nephelometry (Behring); ACPA EliA IgG (Thermo Fisher)



RA= 150; Non-RA = 160
RF Optilite (Binding Site); ACPA IgG BIO-FLASH (Werfen)

Vandebeek *et al.* CCA 2025; 564: 119928
Machold *et al.* ARD 2010; 69: 495-502
Irure-Ventura *et al.* Diagnostics 2025; 15: 135

3.2 Impact of serology on RA classification

RA classification with optimized serological scoring (RCC)

	RA (%)		Non-RA (%)	
	ACR/EULAR 2010	**RCC**	**ACR/EULAR 2010**	**RCC**
Investigative cohort	67.8-74.0	67.1-74.0	7.8-10.5	6.5-6.9
Vandebeek *et al.* (2025)	82.1	82.1	8.6	7.7
Machold *et al.* (2010)	87.1	87.1	21.8	17.6
Irure-Ventura *et al.* (2025)	86.0	82.0	11.9	10.9

- RCC resulted in decreased RA misclassification of non-RA
- RCC minimally affected diagnostic sensitivity

3.2 Impact of serology on RA classification

RCC in seropositive patients

	RA (%)		Non-RA (%)	
	ACR/EULAR 2010	**RCC**	**ACR/EULAR 2010**	**RCC**
Investigative cohort	88.8-90.4	87.2-91.8	38.3-55.8	15.0-25.9
Vandebeek *et al.* (2025)	86.7	86.7	20.0	8.6
Machold *et al.* (2010)	97.3	97.3	79.0	36.8
Irure-Ventura *et al.* (2025)	92.1	87.8	22.6	20.2

- RCC resulted in significantly decreased RA misclassification of seropositive non-RA
- RCC minimally affected diagnostic sensitivity

4. Discussion

Impact of serology in RA classification ↑

ACR/EULAR 2010

Classification criteria for RA (score-based algorithm: add score of categories A–D; a score of ≥6/10 is needed for classification of a patient as having definite RA)‡	
A. Joint involvement§	
1 large joint¶	0
2–10 large joints	1
1–3 small joints (with or without involvement of large joints)#	2
4–10 small joints (with or without involvement of large joints)	3
>10 joints (at least 1 small joint)**	5
B. Serology (at least 1 test result is needed for classification)††	
Negative RF *and* negative ACPA	0
Low-positive RF *or* low-positive ACPA	2
High-positive RF *or* high-positive ACPA	3
C. Acute-phase reactants (at least 1 test result is needed for classification)‡‡	
Normal CRP *and* normal ESR	0
Abnormal CRP *or* abnormal ESR	1
D. Duration of symptoms§§	
<6 weeks	0
≥6 weeks	1

RCC
1-3
3-5

≥ 6/10=RA

RCC results in 5 out of 6 points (83%) in RA classification

Aletaha *et al*. ARD 2010; 69: 1580-8

4. Discussion

4. Discussion

EULAR/ACR risk stratification for 'at risk' RA

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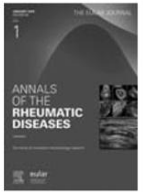


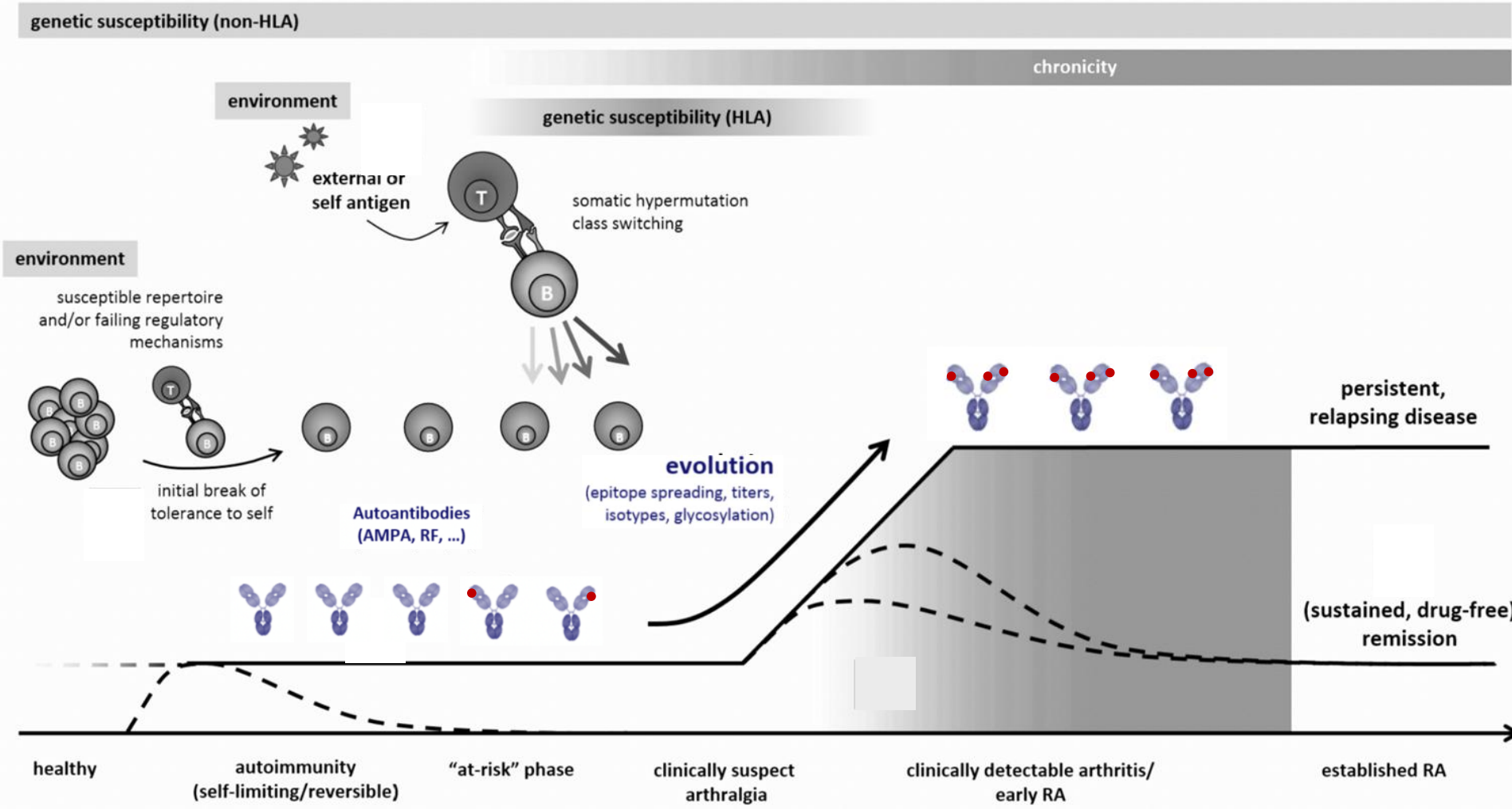
Recommendations

EULAR/ACR risk stratification criteria for development of rheumatoid arthritis in the risk stage of arthralgia

Hanna W. van Steenbergen[1], Frank Doornkamp[2], Stefano Alivernini[3], John Backlund[4], Catalin Codreanu[5], Stanley B. Cohen[6], Bernard Combe[7], Andrew P. Cope[8], Kevin D. Deane[9], Bryant R. England[10], Marie Falahee[11], Pascal H.P. de Jong[12], Arnd Kleyer[13,14], Diane Lacaille[15], Bertha Maat[16], Kulveer Mankia[17], Elise van Mulligen[1,12], György Nagy[18,19,33,34], Liam J. O'Neil[20], Linda Rodamaker[21], Ilfita Sahbudin[11,22], Dirkjan van Schaardenburg[23], Alexandre Sepriano[1,24], Jose A.P. da Silva[25], Lukas De Smet[1], Jeffrey A. Sparks[26], Ewout W. Steyerberg[2], Paul Studenic[27,28], Elisabeth Wethington[29], Robert L. Landewé[30,31], Karim Raza[11,32], Annette H.M. van der Helm-van Mil[1,12,*]

Van Steenbergen*et al*. ARD 2025; doi 10.1016/j.ard.2025.01.021

4. Discussion



Scherer*et al*. J Autoimmun 2020; 110: 102400

4. Discussion

EULAR/ACR risk stratification for 'at risk' RA

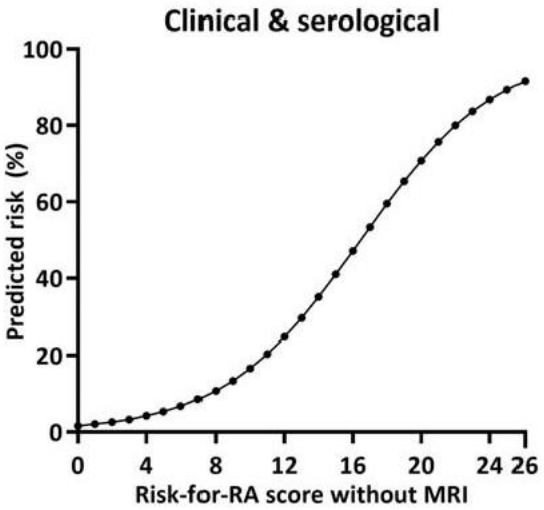
Box EULAR/ACR risk stratification criteria (after simplification) for individuals with arthralgia at risk for RA, to be used in presence or absence of imaging

Target population (who should be tested?): persons with arthralgia in secondary care without clinical arthritis with the arthralgia not better explained by another disease/condition			
Clinical and serologic characteristics		**Score**	
Morning stiffness[a]	0-30 min	0	
	30-60 min	2	
	30-60 min	4	
Patient-reported joint swelling[b]	No	0	
	Yes	4	
Difficulty making a fist[c]	No	0	
	Yes	5	
Increased CRP[d]	No	0	
	Yes	1	
RF[e]	Negative	0	
	Low-positive	2	
	High-positive	4	
ACPA[e]	Negative	0	
	Low-positive	4	
	High-positive	8	
Clinical and serologic sum score		...	*See Figure 2 for risk*
Imaging characteristics if also MRI			
Tenosynovitis flexors wrist[f]	Absent	0	
	Present	6	
Tenosynovitis extensors wrist[g]	Absent	0	
	Present	2	
Tenosynovitis extensors MCPs[h]	Absent	0	
	Present	5	
Tenosynovitis extensors MTPs[i]	Absent	0	
	Present	3	
Subscore MRI		...	
Clinical, serologic, and imaging sum score		...	*See Figure 2 for risk*

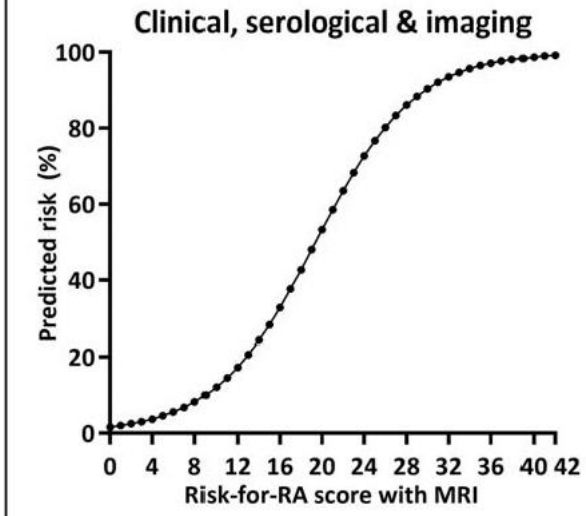
Van Steenbergen*et al*. ARD 2025; doi 10.1016/j.ard.2025.01.021

4. Discussion

EULAR/ACR risk stratification for 'at risk' RA



Cutoff	Sens	Spec	PPV	NPV
≥4 points	95%	14%	23%	97%
≥6 points	90%	38%	26%	96%
≥8 points	78%	50%	33%	94%
≥10 points	66%	71%	38%	92%
≥12 points	51%	80%	46%	90%
≥14 points	37%	91%	53%	88%
≥16 points	24%	94%	60%	86%
≥18 points	13%	98%	64%	85%
≥20 points	7%	99%	71%	84%



Cutoff	Sens	Spec	PPV	NPV
≥5 points	94%	41%	22%	98%
≥8 points	83%	61%	34%	95%
≥10 points	75%	79%	41%	95%
≥12 points	70%	85%	47%	95%
≥15 points	55%	93%	61%	93%
≥18 points	47%	96%	69%	92%
≥20 points	34%	98%	74%	90%
≥22 points	28%	99%	82%	89%
≥24 points	20%	99%	84%	88%

Van Steenbergen*et al*. ARD 2025; doi 10.1016/j.ard.2025.01.021

4. Discussion

EULAR/ACR risk stratification for 'at risk' RA

2010 ACR/EULAR RA classification

ACPA	RF		
	Negative	**Low positive**	**High positive**
Negative	0	2	3
Low positive	2	2	3
High positive	3	3	3

Refined RA classification criteria

ACPA	RF		
	Negative	**Low positive**	**High positive**
Negative	0	0	1
Low positive	1	3	4
High positive	3	4	5

'At risk' RA stratification guidelines

ACPA	RF		
	Negative	**Low positive**	**High positive**
Negative	0	2	4
Low positive	4	6	8
High positive	8	10	12

4. Discussion

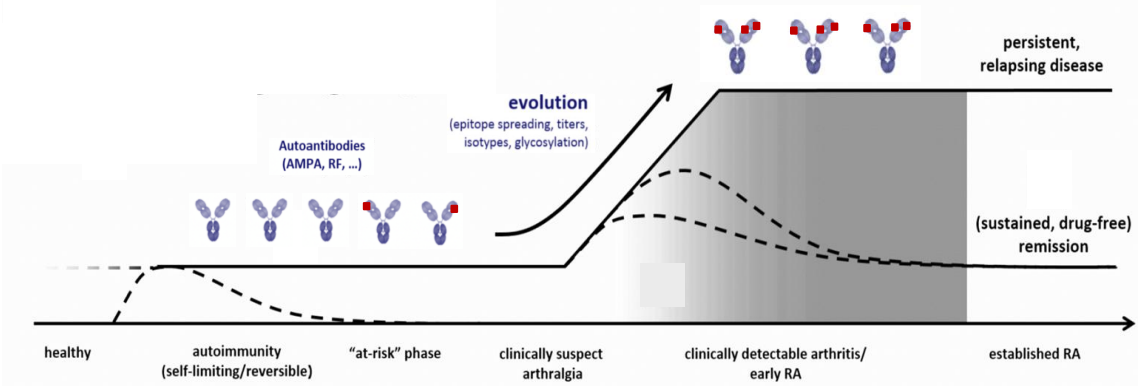
Other points to consider…

- Specificity and gain of RCC significantly differed depending on the study groups

  Clinical diagnosis of all patients was verified 1 or 2 years of (primary diagnostic) study inclusion

  Specificity relates to the number of **'undifferentiated arthritis'** patients in control cohort:

	UA (%) in Non-RA	**% UA in sero pos Non-RA**
Investigative cohort	1 / 448 = 0.2%	0-1 / 28-60 = 1.7%
Vandebeek *et al.* (2025)	8 / 441 = 1.8%	2 / 35 = 5.7%
Machold *et al.* (2010)	96 / 193 = 49.7%	11 / 19 = 57.8%
Irure-Ventura *et al.* (2025)	41 / 160 = 25.6%	32 / 84 = 38.1%



4. Discussion

Other points to consider…

- Specificity and gain of RCC significantly differed depending on the study groups depending on the number of '**seropositive**' patients in control cohort:

	Sero pos (%) in RA	**Sero pos (%) in Non-RA**
Investigative cohort	64.6-74.0%	6.3-14.9%
Vandebeek *et al.* (2025)	67.2%	7.9%
Machold *et al.* (2010)	56.1%	9.8%
Irure-Ventura *et al.* (2025)	92.7%	52.5%

Van Hoovels *et al.* RMD Open 2022; 8: e002099
Vandebeek *et al.* CCA 2025; 564: 119928
Machold *et al.* ARD 2010; 69: 495-502
Irure-Ventura *et al.* Diagnostics 2025; 15: 135

- Criteria use **'ULN'** defined by the manufacturers

  ➡ RA classification depends on the RF/ACPA assay used

Van Hoovels *et al.* J Transl Autoimmun 2022; 5: 100142

  ➡ to be replaced by **uniformized specificity tresholds**

  in order to further harmonize test result interpretation and RA classification

Van Hoovels *et al.* RMD Open 2022; 8: e002099

5. Conclusions and future perspectives

- RF and ACPA are the hallmark antibodies in RA
- LR for RA increases with (i) increasing RF/ACPA Ab concentrations, with (ii) ACPA >> RF and with (iii) double positivity >> single positivity
- An error grid analysis revealed serological scoring weights (upto 5) in line with RF/ACPA Ab impact LR for RA
- Refined RA classification, based on optimized serological scoring, reduces RA misclassification, most significantly in the seropositive subgroup (confirmed on 3 independent study groups)
- (Early) RA classification criteria (should) implement the optimized serological scoring criteria

Thanks to

Collaborators

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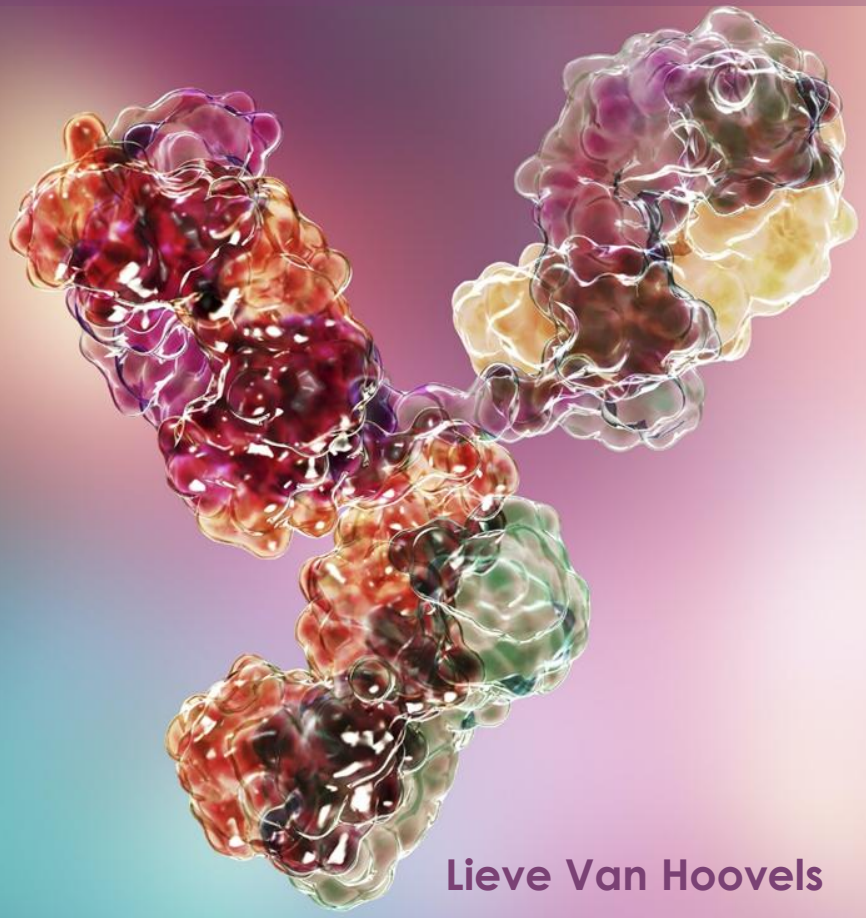
Verschueren P.

Industrial collaborations

Thermo Fisher Scientific
Roche Diagnostics
Orgentec
Abbott
Siemens

It is time to revise RA classification by changing RF and ACPA scores



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AZORO