Erasmus MC
Universitair Medisch Centrum Rotterdam

Nabespreking SKML rondzending Reuma

2010.2, 2011.1, 2011.2

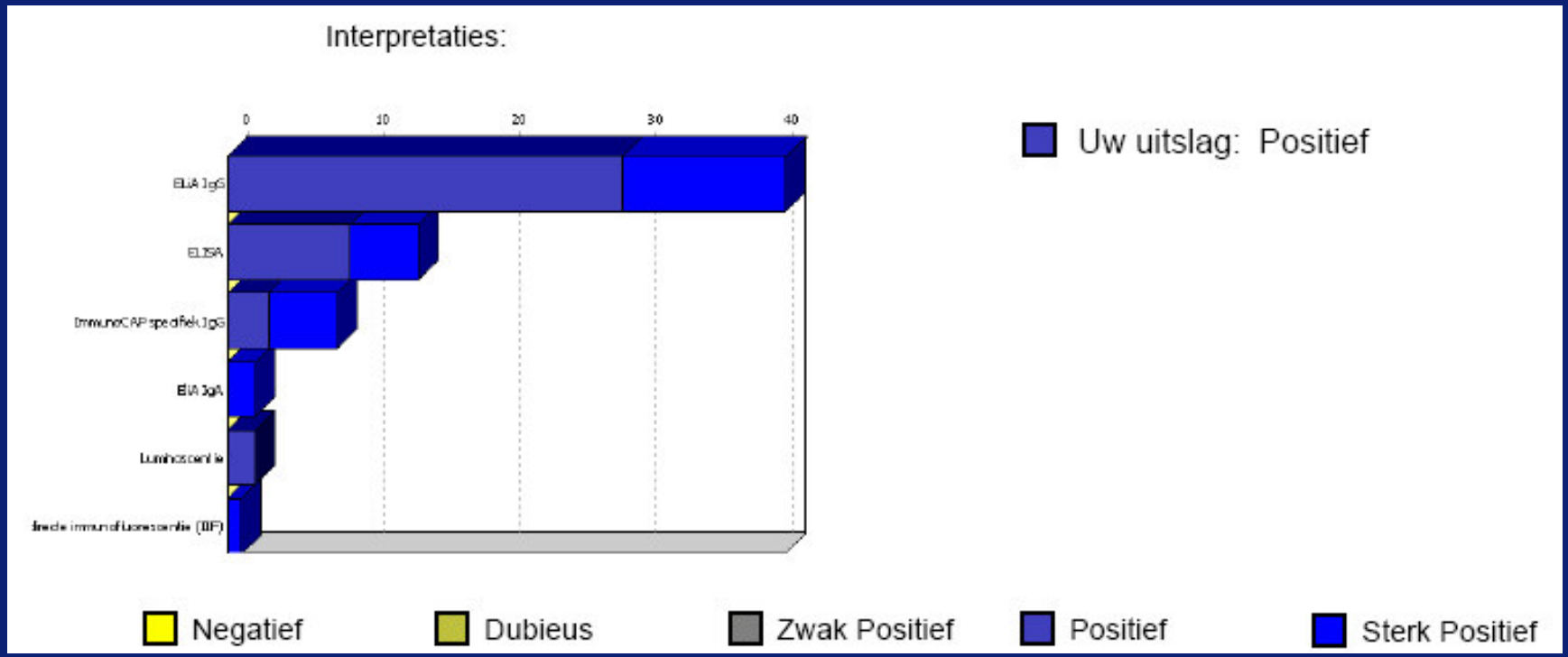
4 april 2012

Marco Schreurs
Immunologie, Erasmus MC

SKML rondzending Reuma

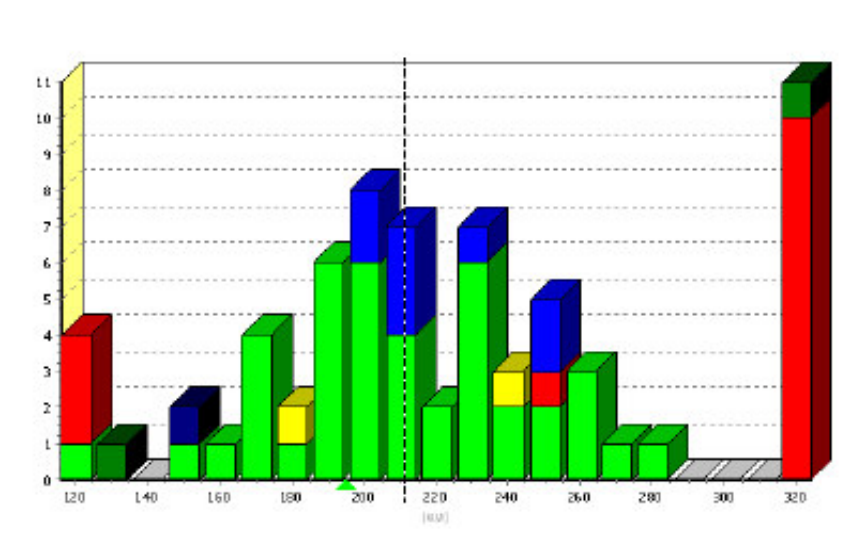
* Voorjaar en najaar, 6 monsters per editie (freeze dried)
* Organisatie: buro SKML, Erasmus MC en SKB, Winterswijk
* Analyse: reumafactor en anti-CCP
* Rapportage: QBase, kwalitatief en kwantitatief
* Terugrapportage: digitaal rapport + commentaar coördinator

QBase: kwalitatieve rapportage



Anti-CCP 2010.2C

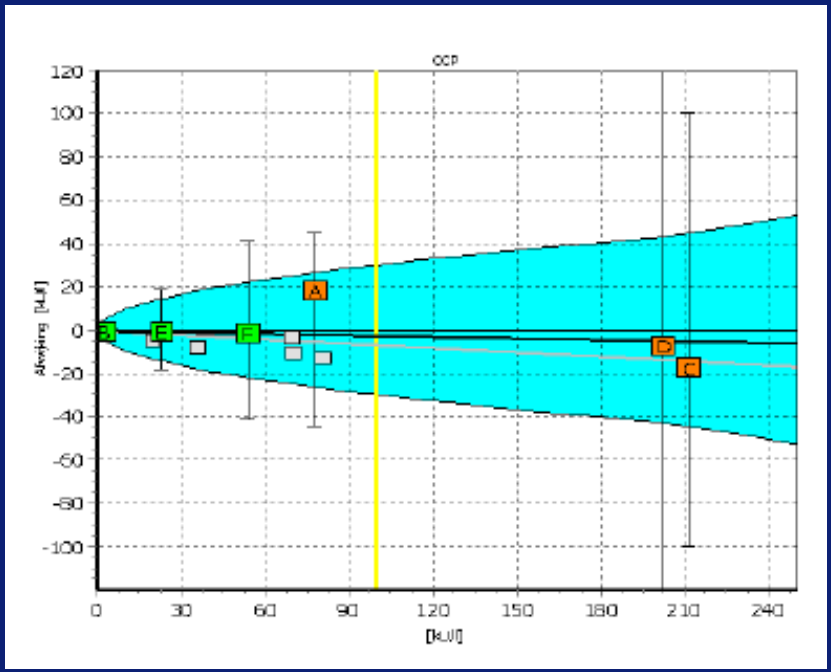
QBase: kwantitatieve rapportage



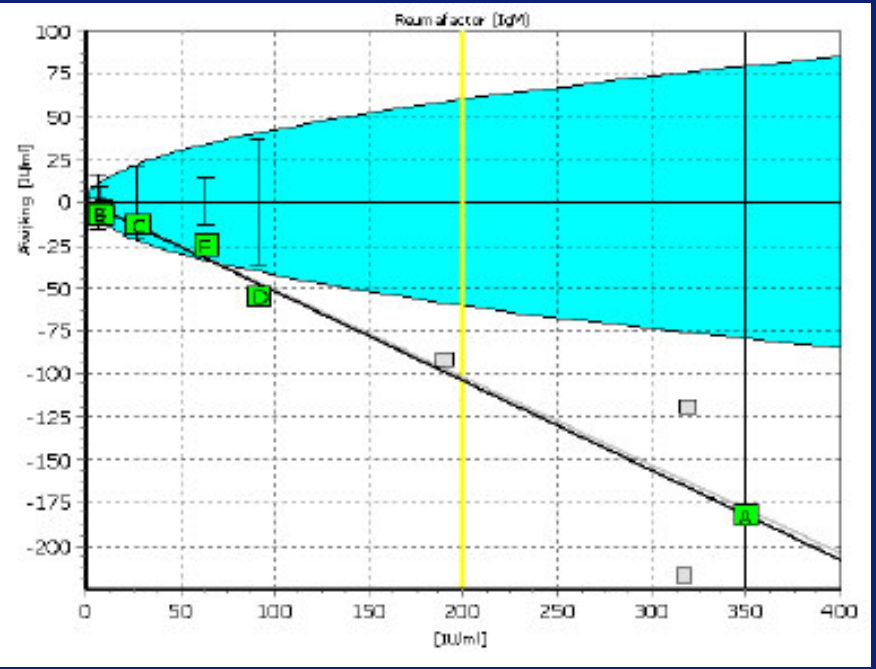
Methode	Gem.	VC	nTot.	nUit.
Overall	210,9	16%	66	13
EliA IgA	207,5		2	0
ELiA IgG	211,6	15%	41	1
ELISA	252,0		13	12
ImmunoCAP specifiek IgG	220,1	10%	8	0
Indirecte immunofluorescentie (IIF)	150,0		1	0
Luminoscentie	131,6		1	0
Uw uitslag	194			

Anti-CCP 2010.2C

QBase: difference plot



Anti-CCP 2010.2



Reumafactor 2010.2

QBase: invoer resultaten

A.U.B. * methode en firma correct invullen
* eenheid correct invullen
* bij negatief resultaat geen getal invullen
* geen < of > resultaat invullen

Anti-CCP 2010.2C

Methode	Gem.	VC	nTot.	nUit.
Overall	210,9	16%	66	13
EliA IgA	207,5		2	0
ELiA IgG	211,6	15%	41	1
ELISA	252,0		13	12
ImmunoCAP specifiek IgG	220,1	10%	8	0
Indirecte immunofluorescentie (IIF)	150,0		1	0
Luminoscentie	131,6		1	0
Uw uitslag	194			

ARTHRITIS & RHEUMATISM
Vol. 62, No. 9, September 2010, pp 2569–2581
DOI 10.1002/art.27584

Arthritis & Rheumatism

An Official Journal of the American College of Rheumatology
www.arthritisrheum.org and www.interscience.wiley.com

2010 Rheumatoid Arthritis Classification Criteria

An American College of Rheumatology/European League Against Rheumatism Collaborative Initiative

Table 3. The 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for rheumatoid arthritis

	Score
Target population (Who should be tested?): Patients who	
1) have at least 1 joint with definite clinical synovitis (swelling)*	
2) with the synovitis not better explained by another disease†	
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

Serologie t.o.v. 1987:

* RF en anti-CCP

* low/high positive (≤/> 3 X ULN)

Nabespreking Reuma
2010.2, 2011.1, 2011.2

Aantal deelnemers Reuma rondzendingen:

Analyse	2010.2	2011.1	2011.2
Reumafactor	84	87	88
Anti-CCP	69	75	75

Reumafactor

Methode	2010.2	2011.1	2011.2
Agglutinatie	2/84	3/87	3/88
Delfia	1/84	1/87	1/88
ELiA IgM	1/84	4/87	10/88
ELISA	13/84	12/87	10/88
Home made assay	2/84	4/87	4/88
Nefelometrie	20/84	18/87	17/88
Turbidimetrie	44/84	45/87	43/88
Indirecte IF*	1/84	0/87	0/88

* Apparaat: overig; Reagens: Phadia (??)

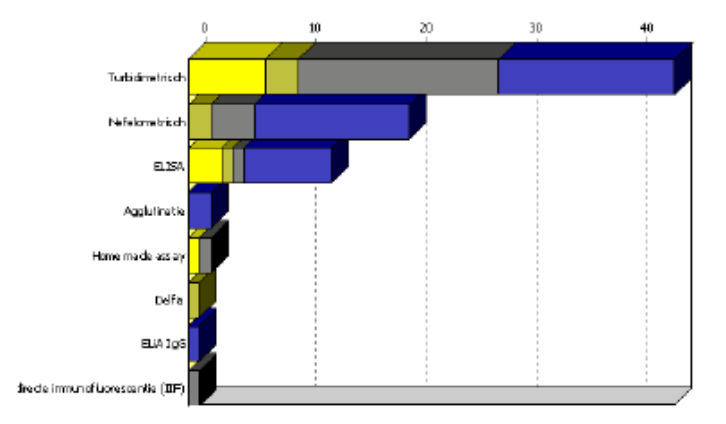
Fundamenteel verschil tussen methoden: bepaling RF-IgM vs. RF-totaal

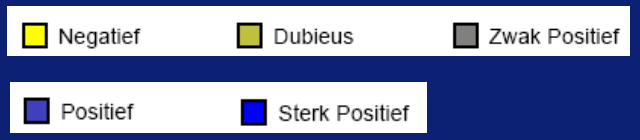
Reumafactor

Kwantitatief (IU/ml):

Rondzending	Monster	Gemiddeld	%VC	Diagnose
2010.2	A	350	33	RA
2010.2	C	27	27	early RA
2010.2	D	92	13	RA
2010.2	F	63	7	SLE, RA?

Kwalitatief: goede consensus, tenmiste bij evident negatief en positief





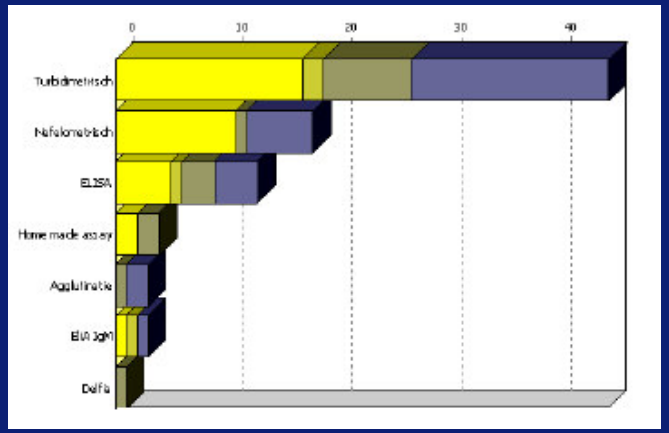
2010.2C

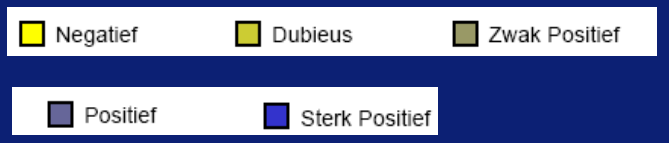
Reumafactor

Kwantitatief (IU/ml):

Rondzending	Monster	Gemiddeld	%VC	Diagnose
2011.1	A	18	32	RA
2011.1	C	30	22	early RA?
2011.1	E	201	52	Sjögren
2011.1	F	288	45	RA

Kwalitatief: goede consensus, tenmiste bij evident negatief en positief





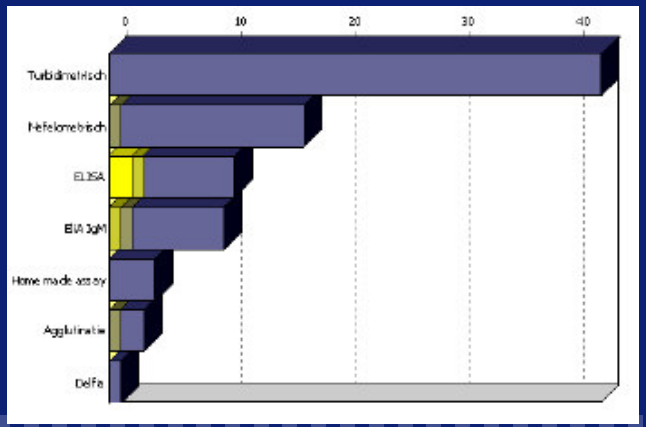
2011.1A

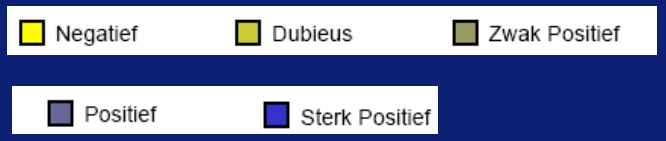
Reumafactor

Kwantitatief (IU/ml):

Rondzending	Monster	Gemiddeld	%VC	Diagnose
2011.2	B	29	15	RA
2011.2	C	61	40	Sjögren
2011.2	D	76	9	RA
2011.2	E	174	22	volgt (AID ?)
2011.2	F	39	47	RA

Kwalitatief: goede consensus, behalve bij ELISA

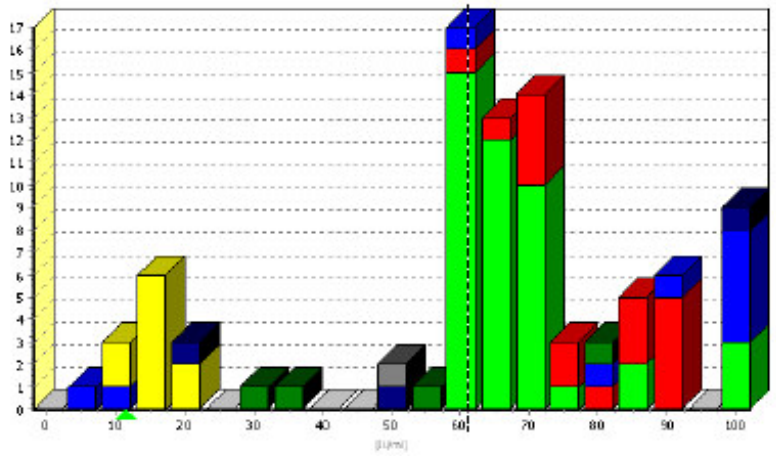




2011.2C

Reumafactor

Monster 2011.2C (vergelijkbaar resultaat bij F)



Methode	Gem.	VC	nTot.	nUit.
Overall	61,2	40%	88	6
Agglutinatie	35,5		3	1
Delfia	48,0		1	0
EliA IgM	15,7	20%	10	0
ELISA	48,6	81%	10	5
Home made assay	50,5		4	0
Nefelometrisch	79,0	13%	17	0
Turbidimetrisch	68,8	18%	43	0
Uw uitslag	11			

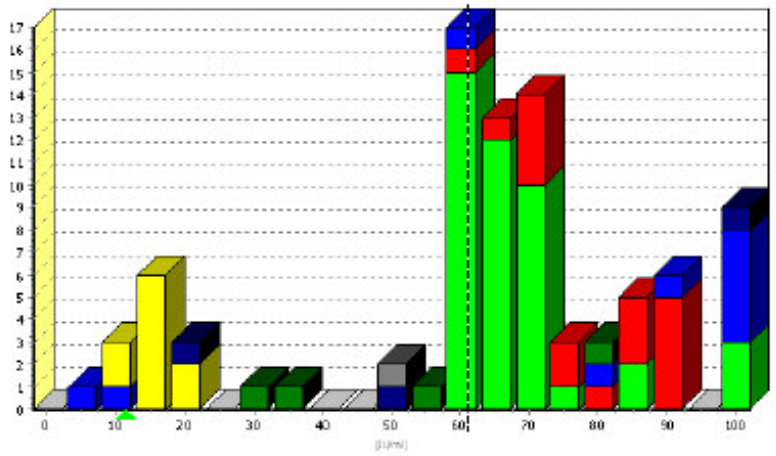
RF-IgM

RF-totaal

ELiA IgM: RF-IgM
Nefelometrie: RF-totaal
Turbidimetrie: RF-totaal

Reumafactor

Monster 2011.2C (vergelijkbaar resultaat bij F)



Methode	Gem.	VC	nTot.	nUit.
Overall	61,2	40%	88	6
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Delfia	48,0		1	0
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Nefelometrisch	79,0	13%	17	0
Turbidimetrisch	68,8	18%	43	0
Uw uitslag	11			

RF-IgM ?

RF-totaal ?

CLB

?

Imtec-IgM

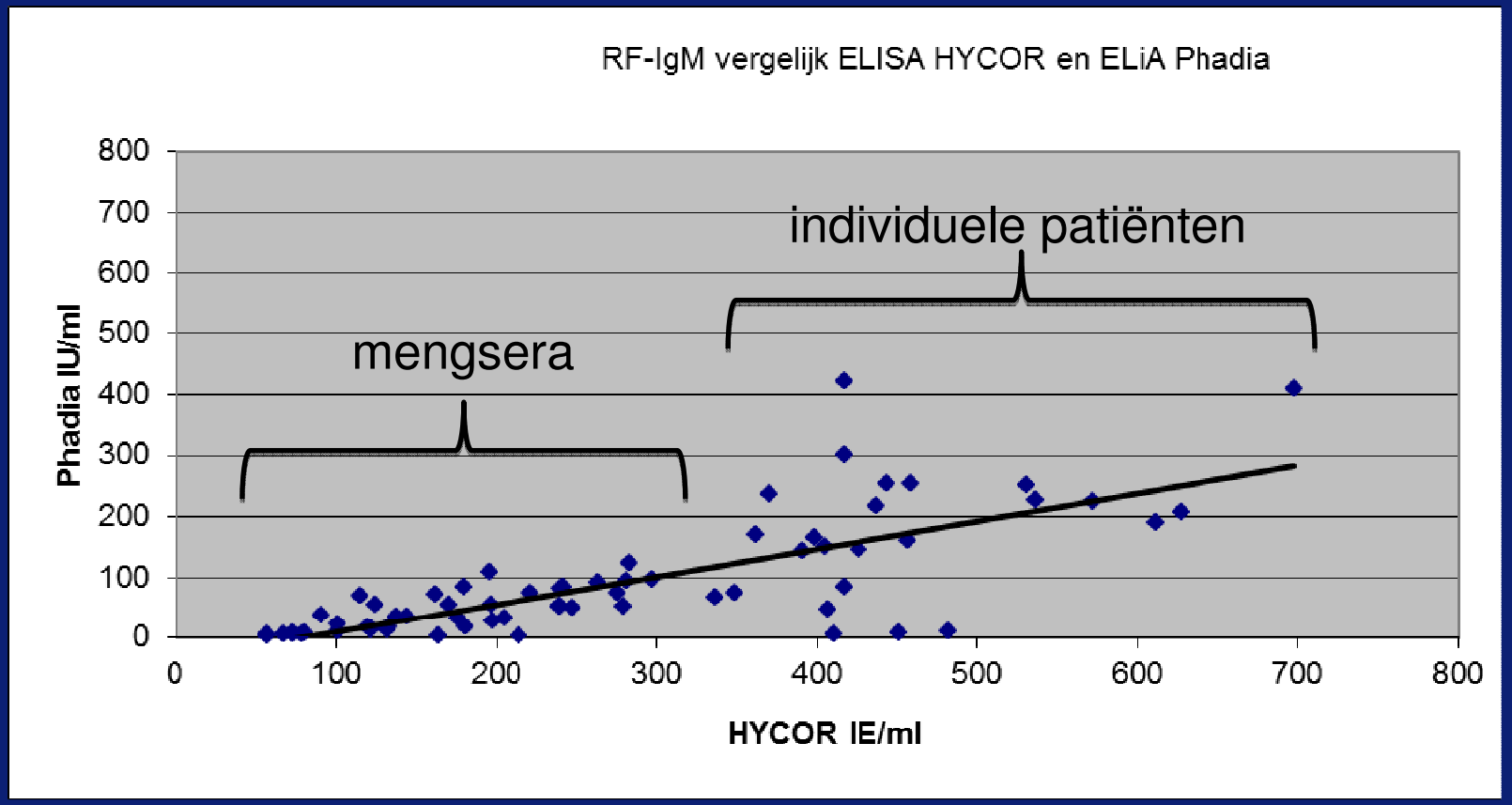
Orgentec IgM/totaal

home made

Hycor IgG/A/M (4), Orgentec (1)

Reumafactor IgM

ELiA vs. Hycor ELISA, zelfde WHO kalibrator



Cut-off Hycor ELISA: 24 IU/ml
Cut-off ELiA: 5 IU/ml

Harmonisatie ?

Harmonisatie

Het harmoniseren van methoden: het bereiken van uniforme uitslagen op verschillende labs, tussen methoden welke gekalibreerd zijn met dezelfde standaard.

Lijkt niet mogelijk voor reumafactor !

Verschillende methoden meten verschillende (sub)populaties van RF, hetgeen per patiënt en per methode verschillende resultaten oplevert.

Voor meer info:
www.skml.nl
Presentatie Cas Weykamp: Het omgekeerde schaakspel
SKML congres: Kwaliteit in Harmonisatie, 14 juni 2011

Reumafactor totaal

Nefelo- vs. turbidimetrie, zelfde WHO kalibrator

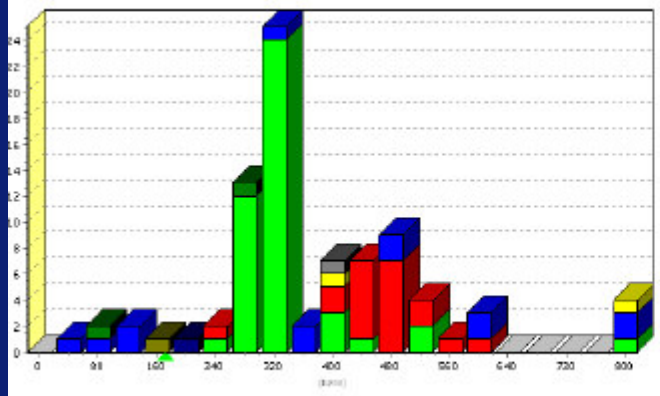
Clin Rheumatol
DOI 10.1007/s10067-011-1716-3

ORIGINAL ARTICLE

Rheumatoid factor measurement—continuing problems 70 years after discovery

Rohan Ameratunga · Samarina Musaad · Claudia Sugrue · Campbell Kyle

Standardization for RF measurement is not optimal and has not been achieved between these two commonly used instruments. This may have clinical implications for patient management.



Methode	Gem.	VC	nTot.	nUit.
Overall	350,0	33%	81	1
Agglutinatie	400,0		2	1
Delfia	390,0		1	0
ELiA IgG	168,0		1	0
ELISA	330,9	63%	11	0
Home made assay	180,0		2	0
Indirecte immunofluorescentie (IIF)	188,0		1	0
Nefelometrisch	454,4	16%	20	0
Turbidimetrisch	320,1	18%	43	0
Uw uitslag	168			

2010.2A

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Arthritis & Rheumatism

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Normal CRP *and* normal ESR	0
Abnormal CRP *or* abnormal ESR	1
D. Duration of symptoms§§	
<6 weeks	0
≥6 weeks	1

Serologie t.o.v. 1987:

* RF en anti-CCP

* low/high positive (≤/> 3 X ULN)

ARTHRITIS & RHEUMATISM
Vol. 63, No. 5, May 2011, pp 1190–1199
DOI 10.1002/art.30200

Erasmus MC

Toward a Data-Driven Evaluation of the 2010 American College of Rheumatology/European League Against Rheumatism Criteria for Rheumatoid Arthritis

Is It Sensible to Look at Levels of Rheumatoid Factor?

M. P. M. van der Linden,[1] M. R. Batstra,[2] L. E. Bakker-Jonges[2] on behalf of the Foundation for Quality Medical Laboratory Diagnostics, J. Detert,[3] H. Bastian,[3] H. U. Scherer,[4] R. E. M. Toes,[1] G.-R. Burmester,[3] M. D. Mjaavatten,[5] T. K. Kvien,[5] T. W. J. Huizinga,[1] and A. H. M. van der Helm-van Mil[1]

Conclusion. **Our findings indicate that determination of RF level is subject to large variation; high RF level has limited additive prognostic value compared to ACPA positivity. Thus, omitting RF level and using RF presence, ACPA presence, and ACPA level may improve the 2010 criteria for RA.**

Anti-CCP

Methode	2010.2	2011.1	2011.2
ELiA IgA*	2/69	2/75	1/75
ELiA IgG	41/69	48/75	48/75
ELISA	14/69	13/75	14/75
ImmunoCAP specifiek IgG*	8/69	7/75	7/75
Luminoscentie	3/69	4/75	4/75
Indirecte IF**	1/69	1/75	1/75

* Foutieve methode invoer: moet zijn ELiA IgG
* * Foutieve methode invoer: Apparaat = Abbott AxSym

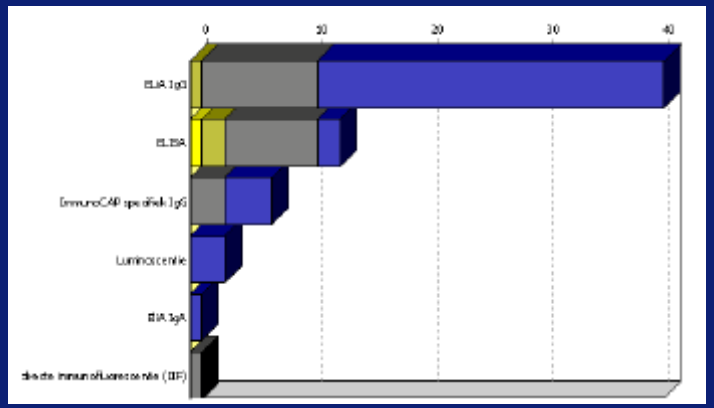
ELiA IgG: 74% van de deelnemers !

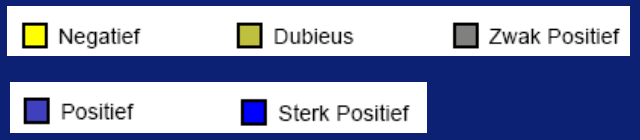
Anti-CCP

Kwantitatief (U/ml, kU/l):

Rondzending	Monster	Gemiddeld	%VC	Diagnose
2010.2	A	78	19	RA
2010.2	C	211	16	early RA
2010.2	D	202	34	RA
2010.2	E	23	28	early RA ??
2010.2	F	54	25	SLE, RA?

Kwalitatief: goede consensus, muv enkel laag positief monster





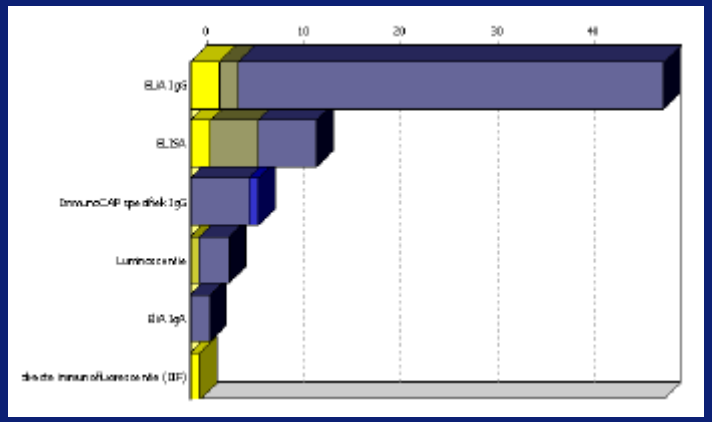
2010.2E

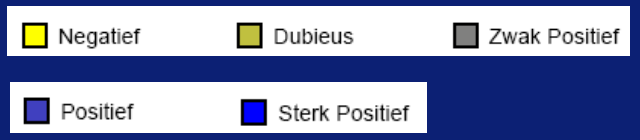
Anti-CCP

Kwantitatief (U/ml, kU/l):

Rondzending	Monster	Gemiddeld	%VC	Diagnose
2011.1	A	42	25	RA
2011.1	C	26	40	early RA ?
2011.1	D	294	26	RA
2011.1	F	1614	82	RA

Kwalitatief: goede consensus, muv enkel laag positief monster





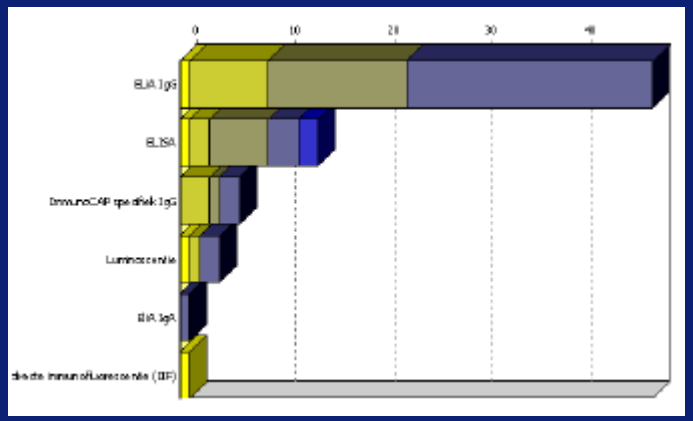
2011.1C

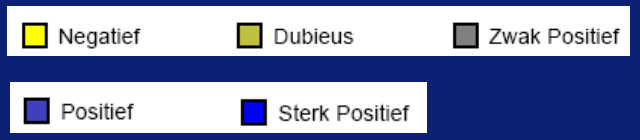
Anti-CCP

Kwantitatief (U/ml, kU/l):

Rondzending	Monster	Gemiddeld	%VC	Diagnose
2011.2	B	361	24	RA
2011.2	D	18	25	RA
2011.2	E	12	22	AID ?
2011.2	F	1111	53	RA

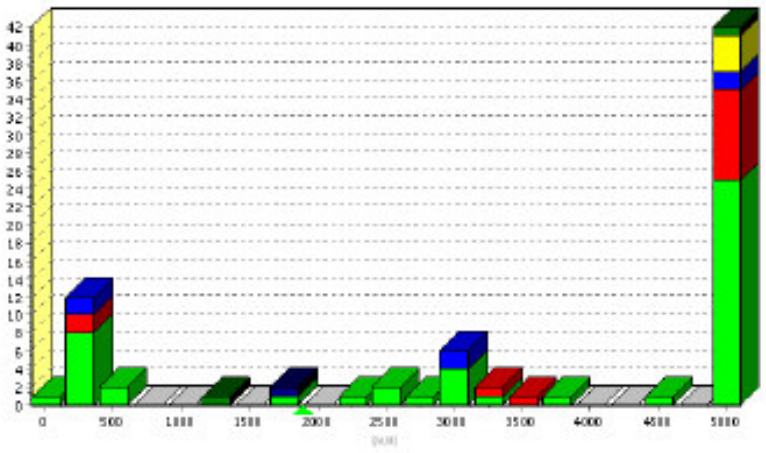
Kwalitatief: goede consensus, muv enkel laag positief monster





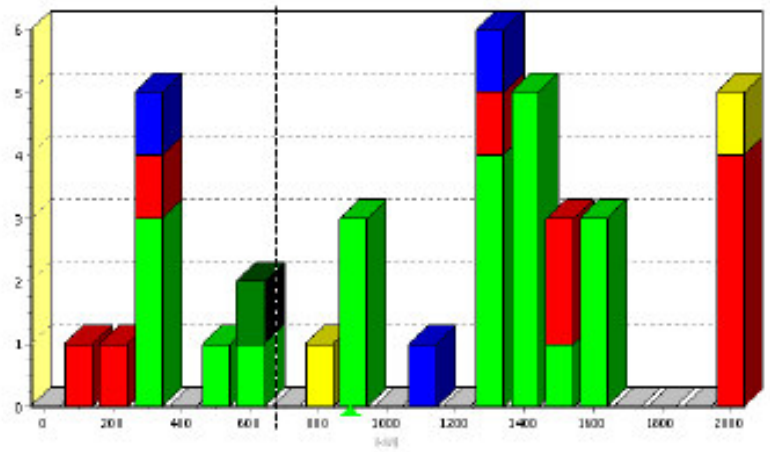
2011.2E

Anti-CCP +++



Methode	Gem.	VC	nTot.	nUit.
Overall	1614,1	82%	34	2
EliA IgA	1360,0		1	0
ELiA IgG	1577,0	84%	22	0
ELISA	1789,5	101%	6	2
ImmunoCAP specifiek IgG	1664,5		4	0
Indirecte immunofluorescentie (IIF)	1780,0		1	0
Uw uitslag	1867			

2011.1F

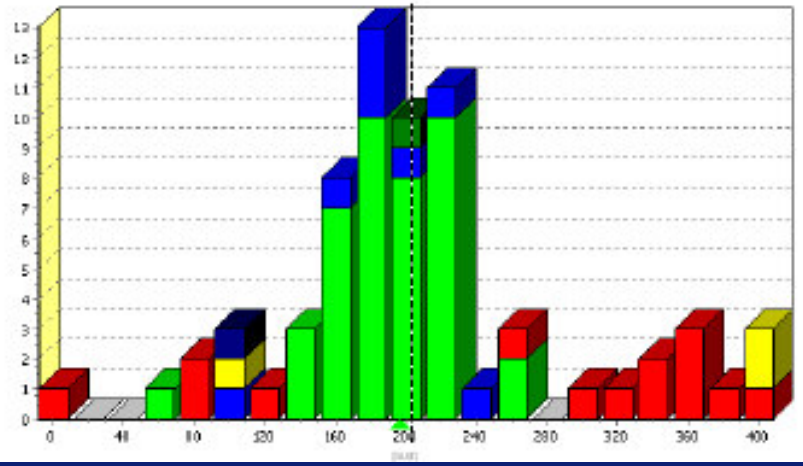


Methode	Gem.	VC	nTot.	nUit.
Overall	1111,4	53%	37	2
ELiA IgG	1106,3	41%	21	0
ELISA	1284,0	69%	10	1
ImmunoCAP specifiek IgG	914,3		3	0
Indirecte immunofluorescentie (IIF)	610,0		1	0
Luminoscentie	758,0		2	1
Uw uitslag	882			

2011.2F

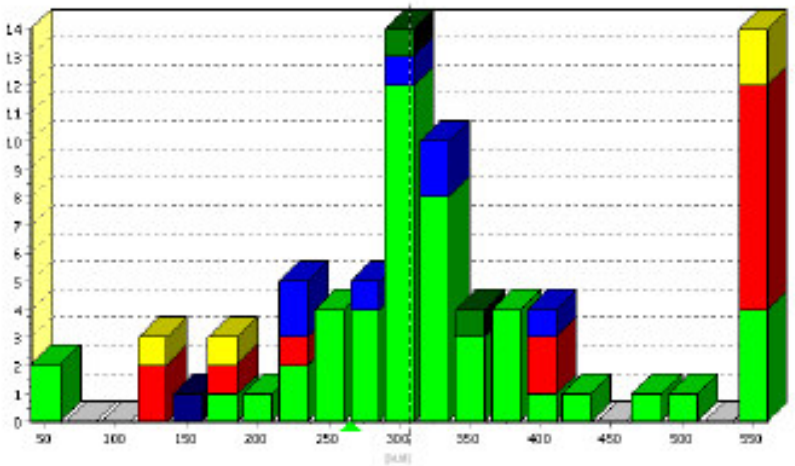
> 50% deelnemers voert >max bereik in. A.U.B. verdund hertesten !

Anti-CCP ELISA



Methode	Gem.	VC	nTot.	nUit.
Overall	201,6	34%	66	2
EliA IgA	194,0		1	0
ELiA IgG	189,3	19%	41	0
ELISA	273,6	42%	14	2
ImmunoCAP specifiek IgG	183,1	21%	8	0
Indirecte immunofluorescentie (IIF)	105,0		1	0
Luminoscentie	95,3		1	0
Uw uitslag	195			

2010.2D



Methode	Gem.	VC	nTot.	nUit.
Overall	293,7	26%	71	11
EliA IgA	328,0		2	0
ELiA IgG	309,6	19%	45	3
ELISA	242,9	51%	14	8
ImmunoCAP specifiek IgG	294,4	22%	7	0
Indirecte immunofluorescentie (IIF)	157,0		1	0
Luminoscentie	145,2		2	0
Uw uitslag	263			

2011.1D

Anti-CCP ELISA

Fabrikant	Cut-off U/ml	Aantal deelnemers
Eurodiagnostica	25	8
Biorad	1	1
Inova	20	1
EuroImmun	5	1
Axis-Shield	50	1
Siemens	20	1
Abbott	5	1

Variatie uitslagen tussen fabrikanten, vanwege gebrek aan uniforme kalibratie, maar ook binnen fabrikant

Anti-CCP laat zich echter wel harmoniseren, mits gebruik van een kalibrator

Voor meer info:
www.skml.nl
Presentatie Cas Weykamp: Het omgekeerde schaakspel
SKML congres: Kwaliteit in Harmonisatie, 14 juni 2011

Conclusie

Over het algemeen goede consensus

Variatie in kwalitatieve resultaten bij zwak positieve monsters

Variatie in kwantitatieve resultaten door verschillen in meetmethoden en harmonisatie probleem (RF), dan wel door gebrek aan uniforme kalibratie (anti-CCP ELISA)

Invoer methoden voor verbetering vatbaar

Verdund hertesten van hoog positieven noodzakelijk

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