From ANA to ENA: detection algorithms in the Netherlands

Jan Damoiseaux

European Autoantibody Standardization Initiative

Goals:

- Optimizing communication between clinicians and laboratory specialists,
- Establishing international standard preparations for autoantibody tests,
- Harmonizing testing algorithms.

Shoenfeld et al.
ANYAS 1109: 138-144 (2007)

Damoiseaux et al.
ANYAS 1173: 10-14 (2009)

Questionnaire

Categories:

- Organisation (n=4),
- ANA testing (n=14),
- Anti-dsDNA ab testing (n=8),
- Anti-ENA ab testing (n=15),
- ANA/ENA algorithm (n=16).

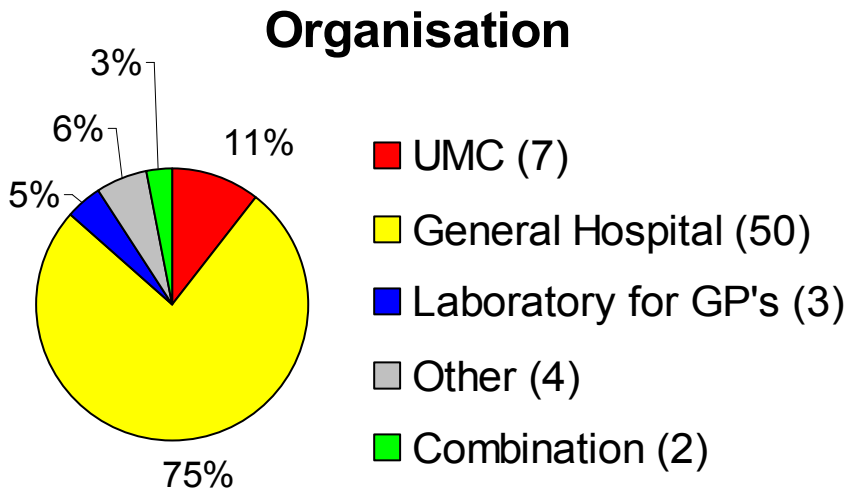
Response

Send out to 81 laboratories:

- Dutch diagnostic laboratories (n=76),
- Foreign diagnostic laboratories (n=2),
- Diagnostic compagnies (n=3),

→ 66 questionnaires were returned (87%)

Organisation



Organisation

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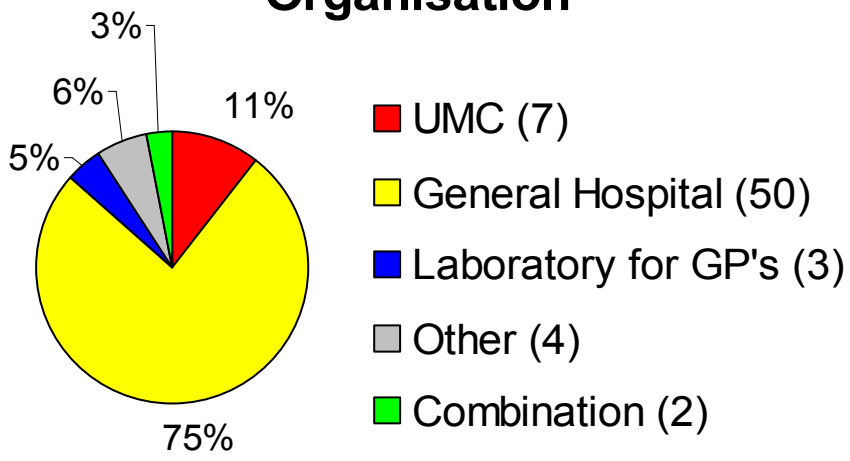
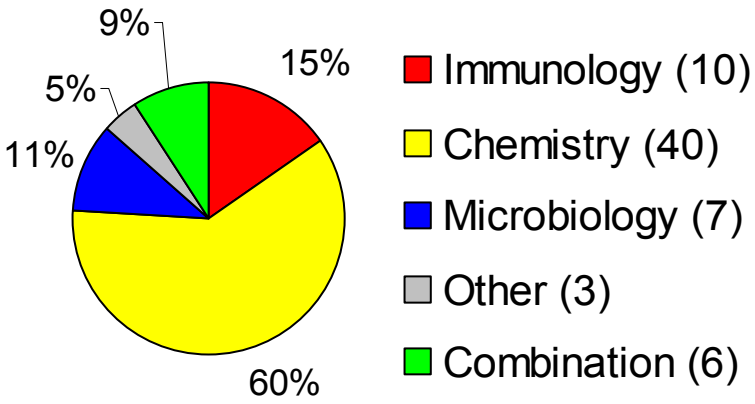


Laboratory type



Organisation

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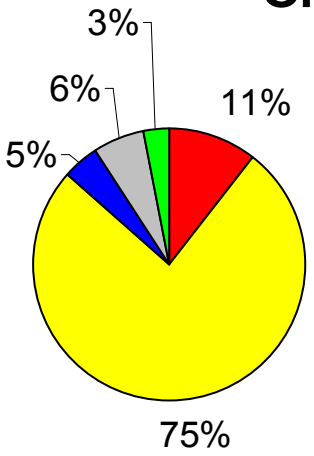
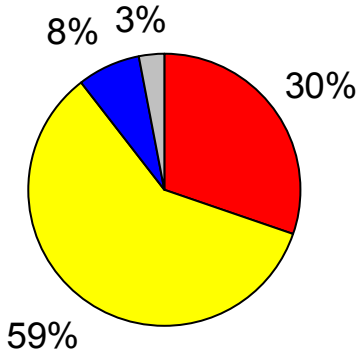


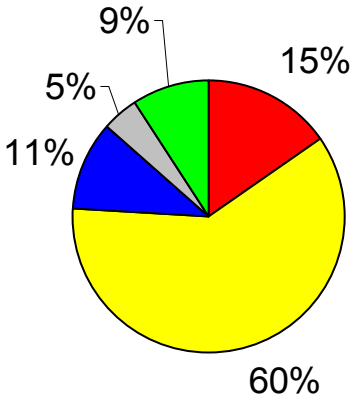
- UMC (7)
- General Hospital (50)
- Laboratory for GP's (3)
- Other (4)
- Combination (2)

Laboratory specialist



- Immunologist (20)
- Chemist (39)
- Microbiologist (5)
- Other (2)

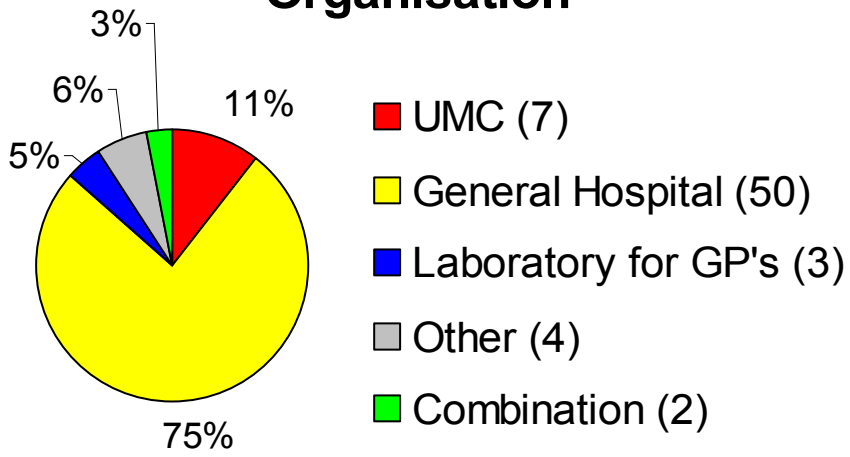
Laboratory type



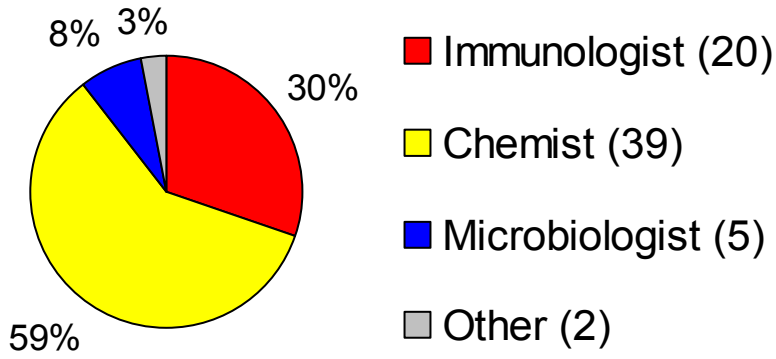
- Immunology (10)
- Chemistry (40)
- Microbiology (7)
- Other (3)
- Combination (6)

Organisation

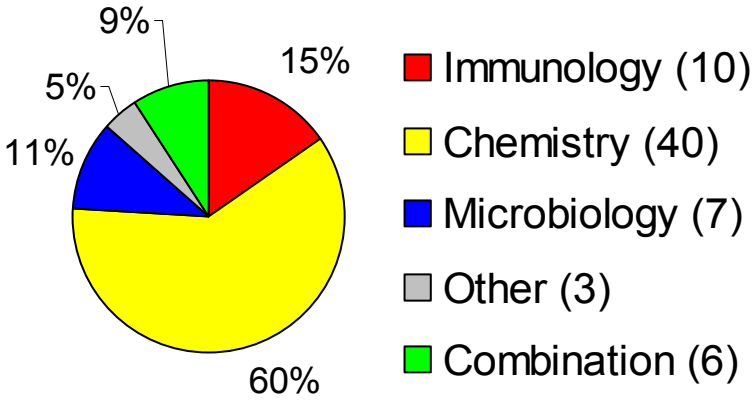
Organisation



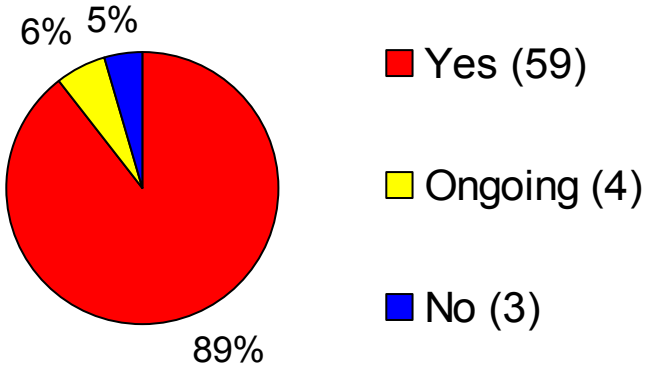
Laboratory specialist



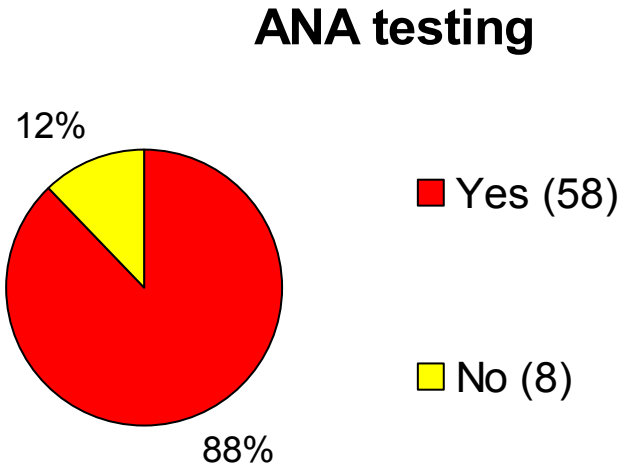
Laboratory type



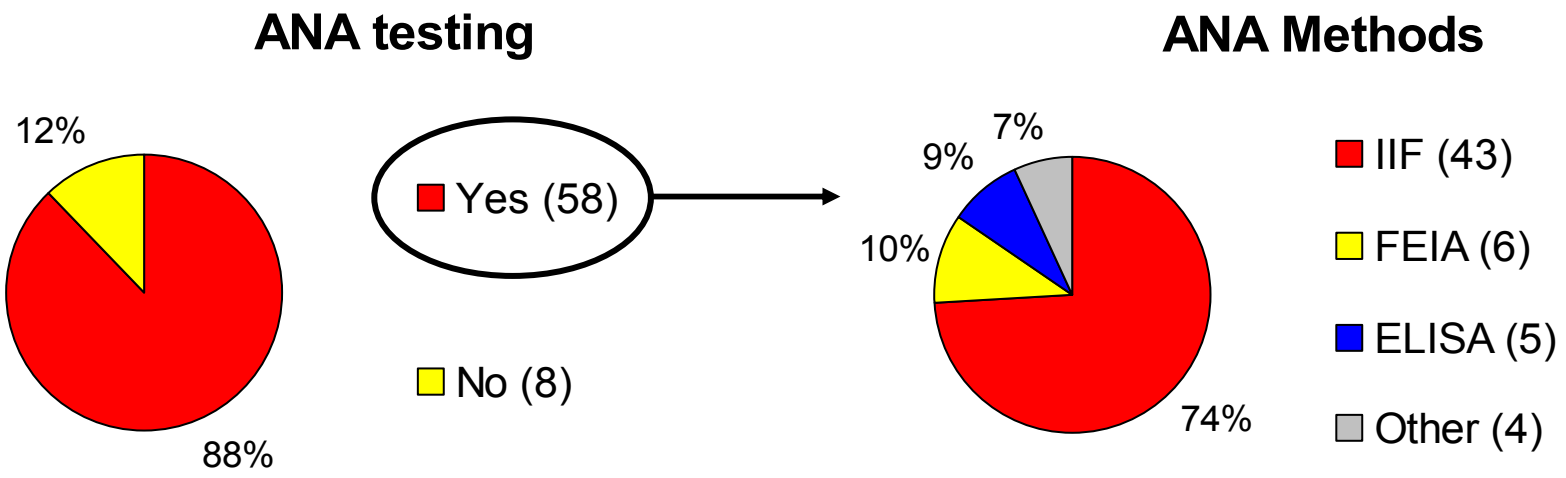
Accreditation



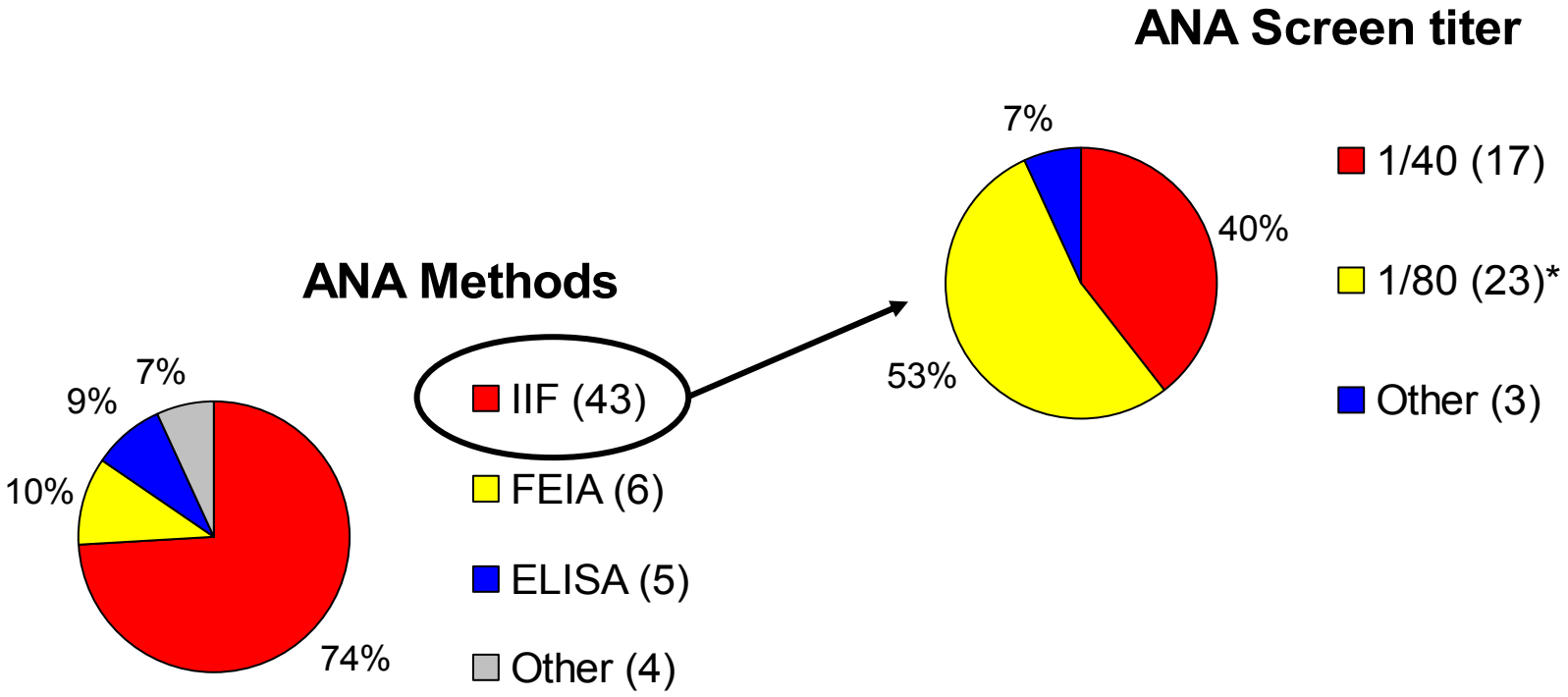
ANA testing



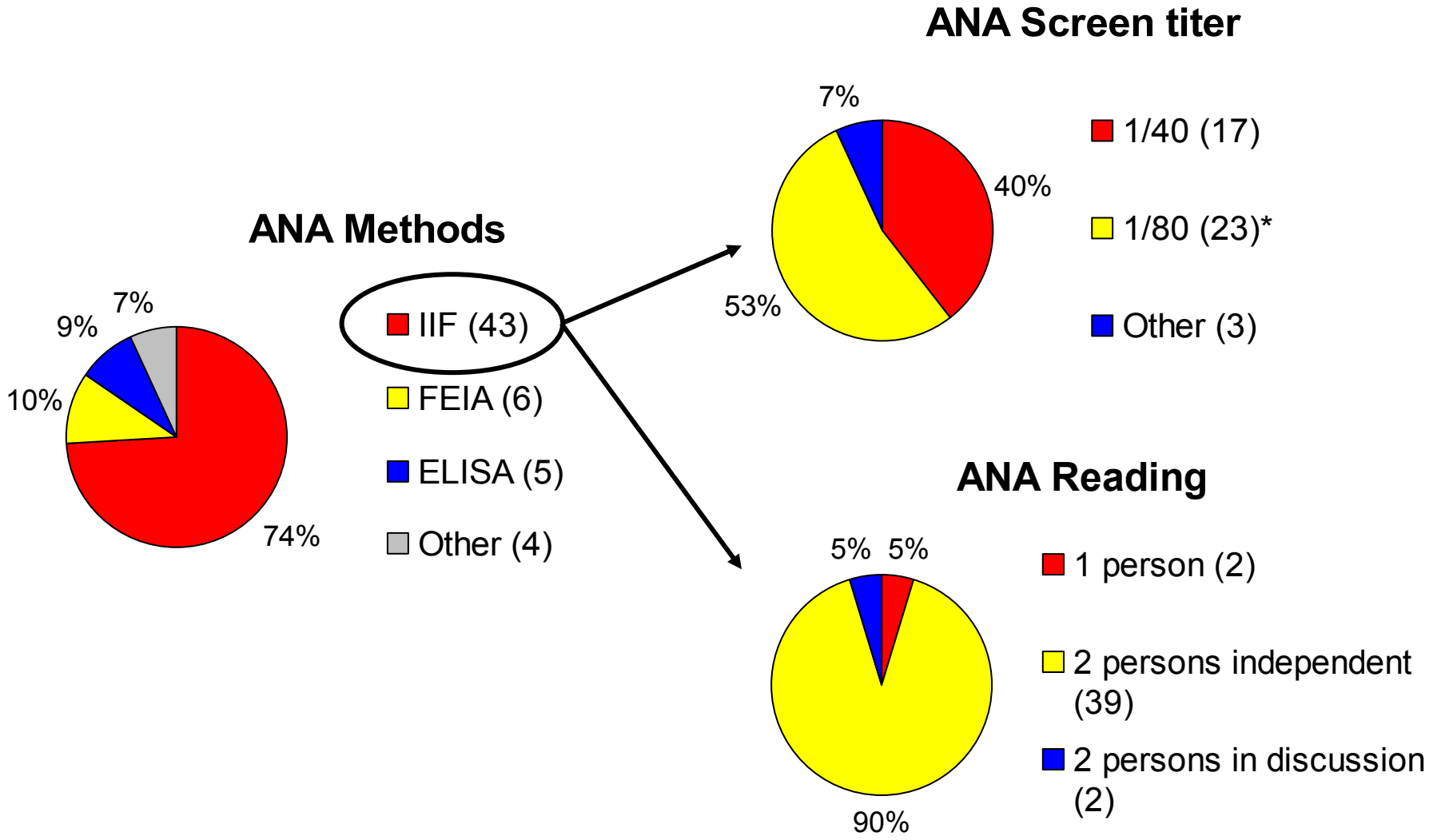
ANA methods


ANA testing
12%
88%
Yes (58)
No (8)
ANA Methods
7%
9%
10%
74%
IIF (43)
FEIA (6)
ELISA (5)
Other (4)

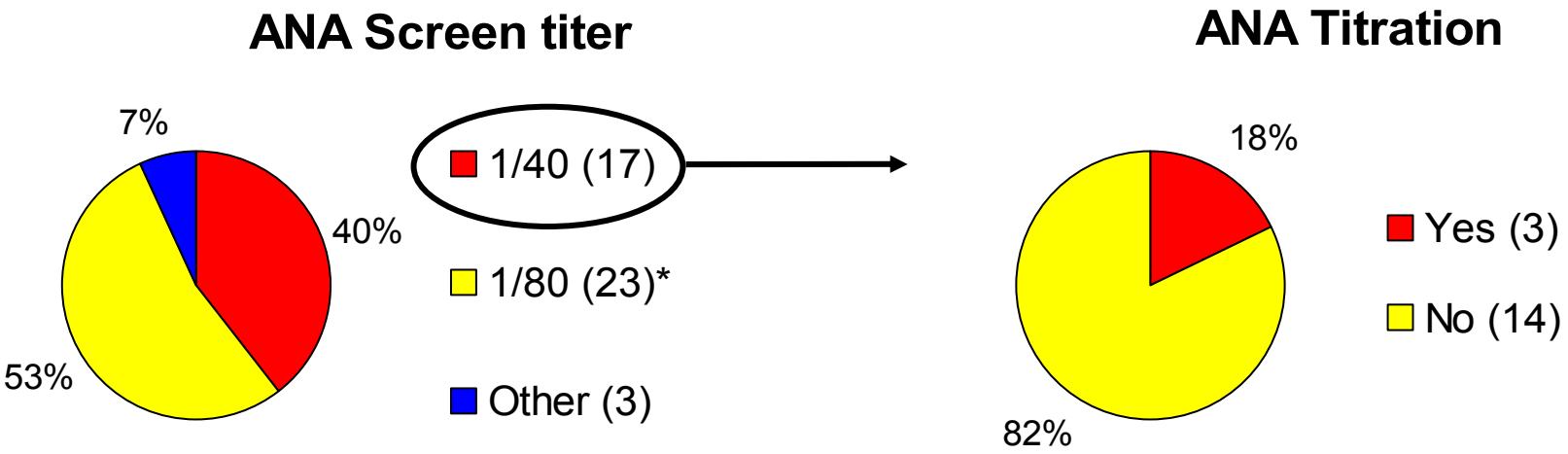
ANA testing


ANA Methods
IIF (43)
FEIA (6)
ELISA (5)
Other (4)
74%
10%
9%
7%
ANA Screen titer
1/40 (17)
1/80 (23)*
Other (3)
40%
53%
7%

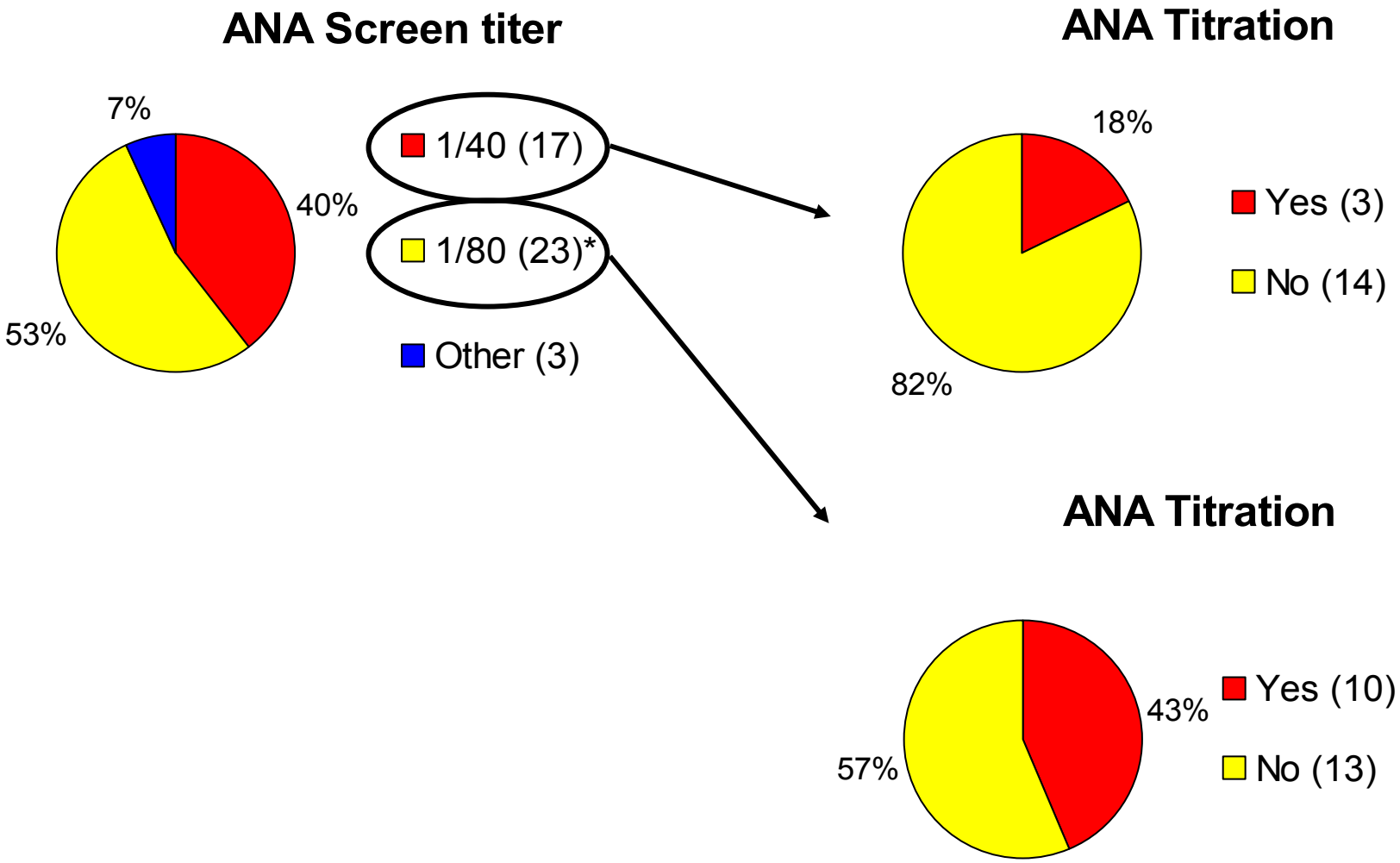
ANA testing


ANA Screen titer
7%
40%
53%
1/40 (17)
1/80 (23)*
Other (3)
ANA Methods
IIF (43)
FEIA (6)
ELISA (5)
Other (4)
7%
9%
10%
74%
ANA Reading
5% 5%
90%
1 person (2)
2 persons independent (39)
2 persons in discussion (2)

ANA titration



ANA titration



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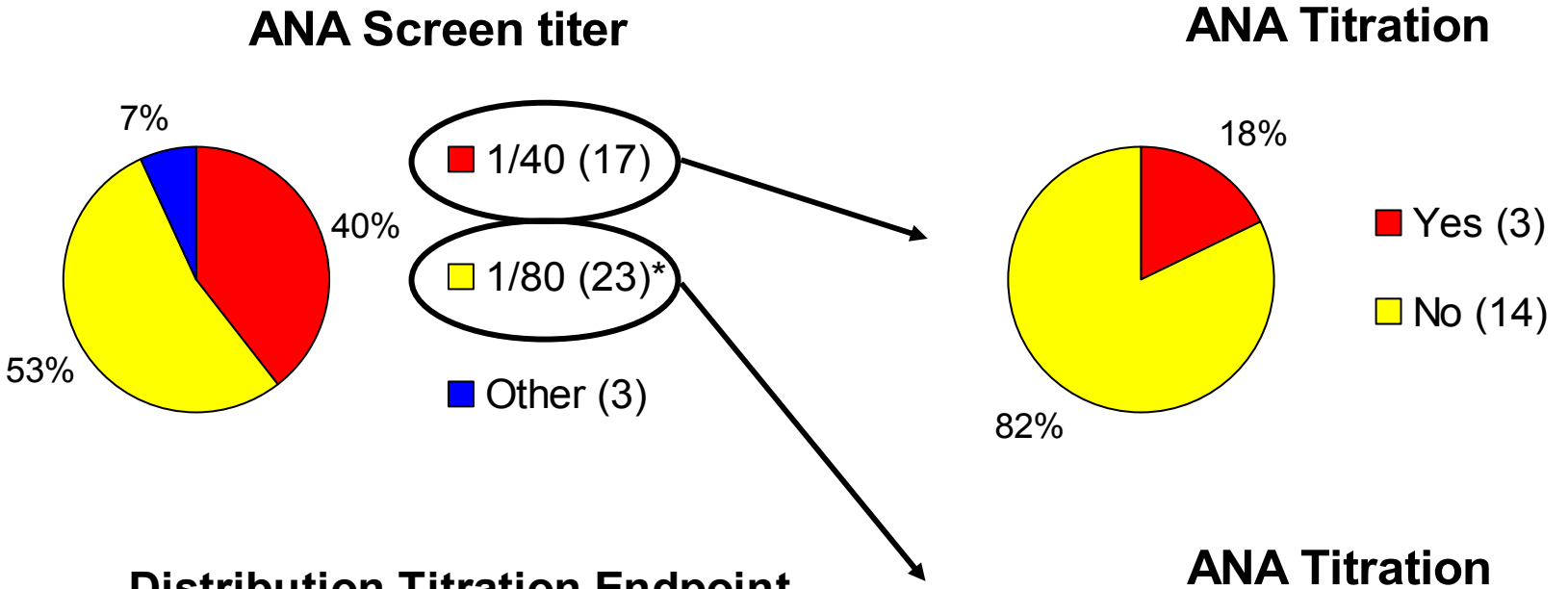
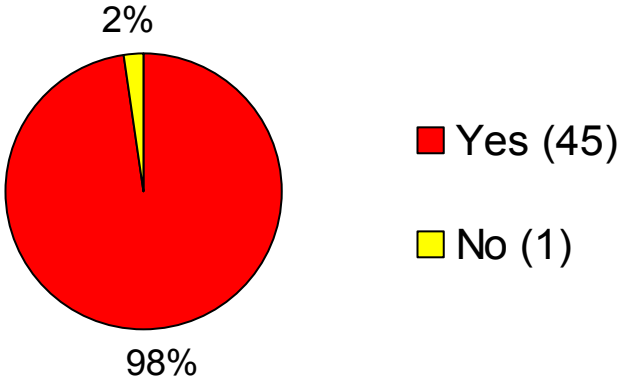


ANA pattern

ANA Fluorescent pattern



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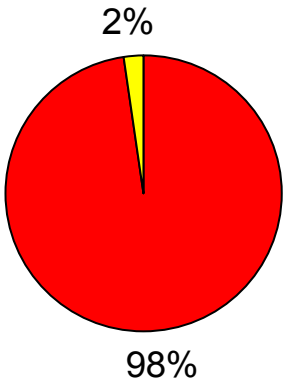
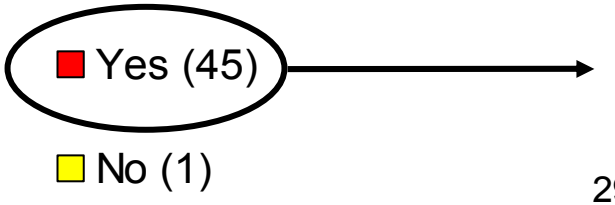
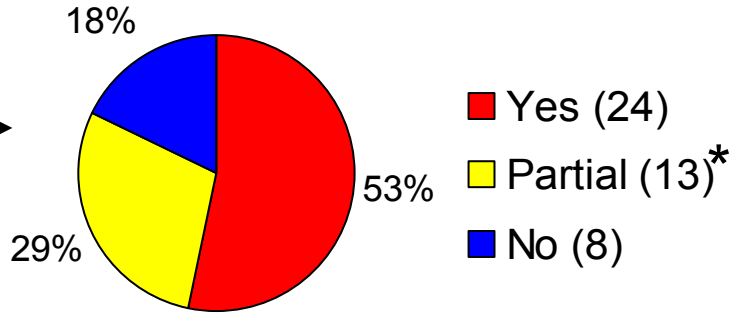


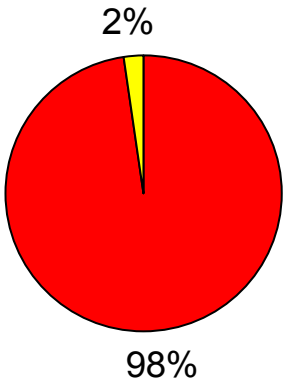


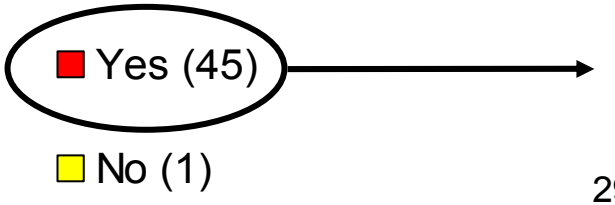
ANA Pattern report



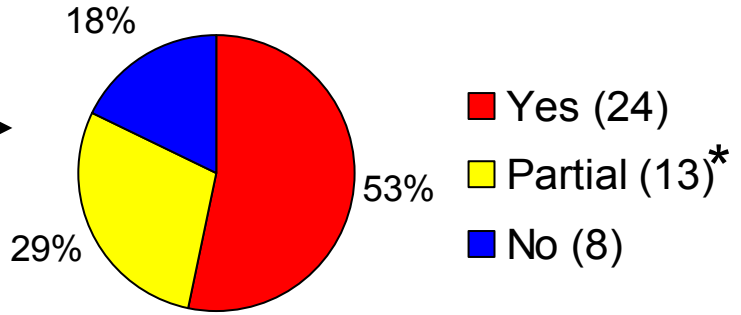
ANA pattern

ANA Fluorescent pattern

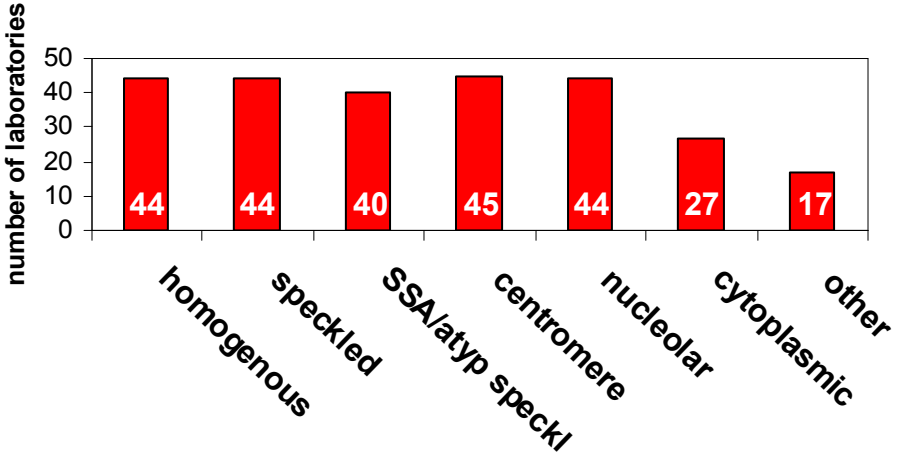




ANA Pattern report

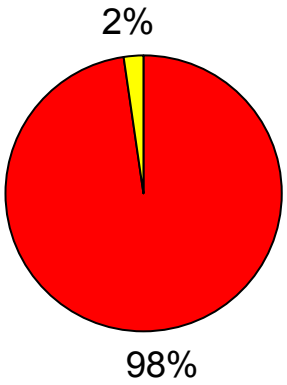


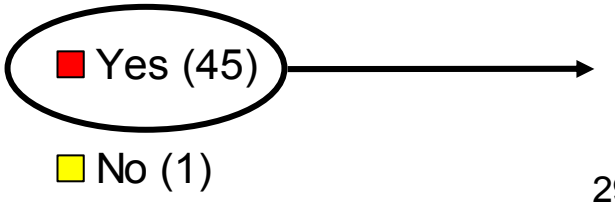
ANA Pattern distinction



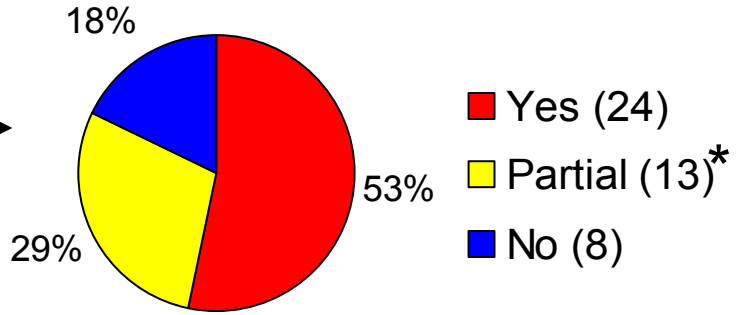
ANA pattern

ANA Fluorescent pattern

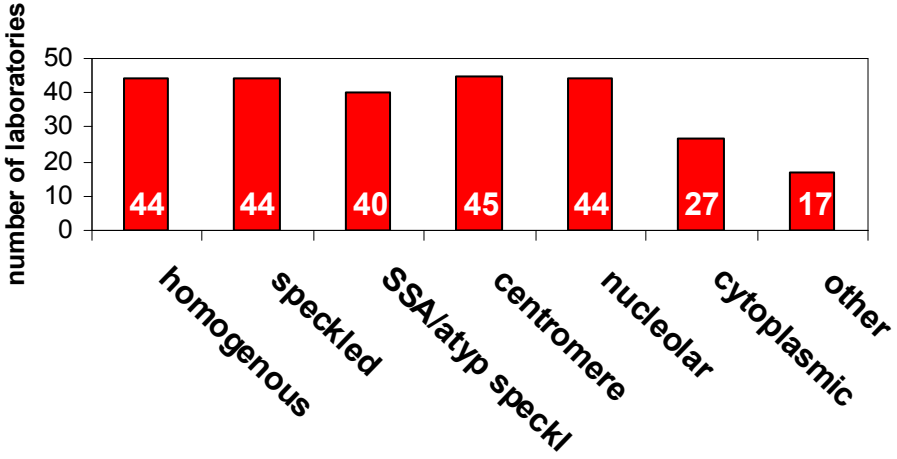




ANA Pattern report

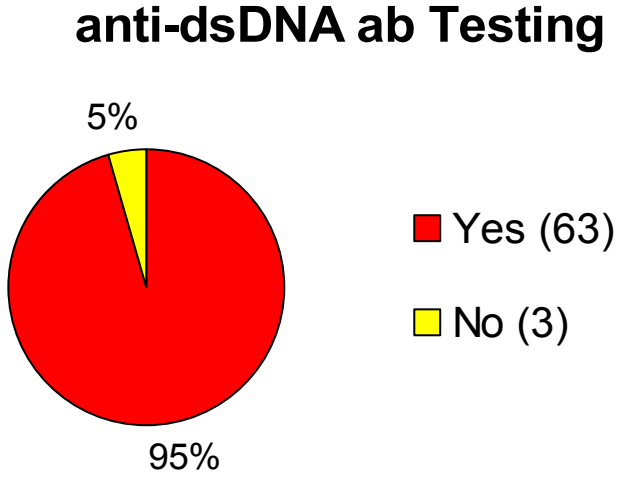


ANA Pattern distinction

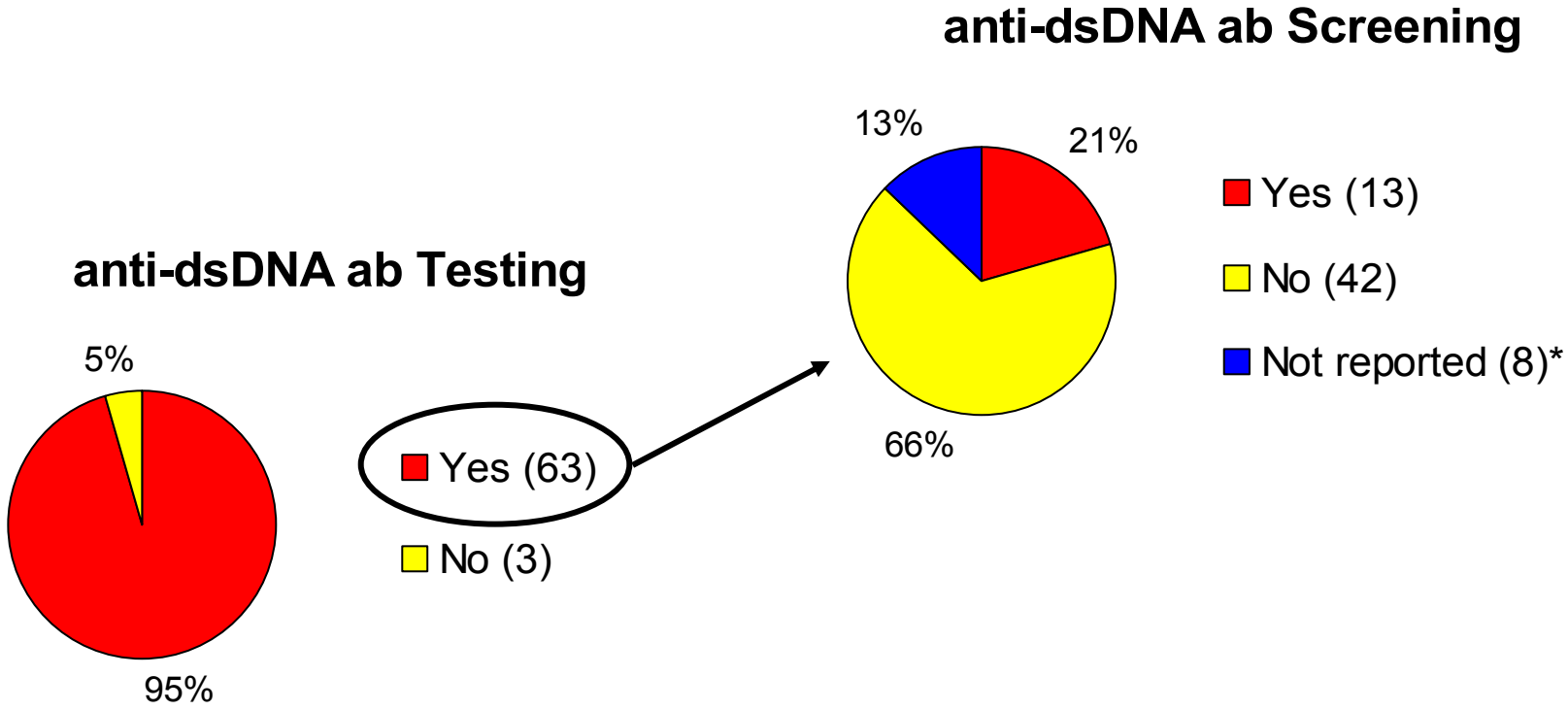


Pattern	Number
Nuclear dots	13
Nuclear membrane	10
Nuclear matrix	4
PCNA	4

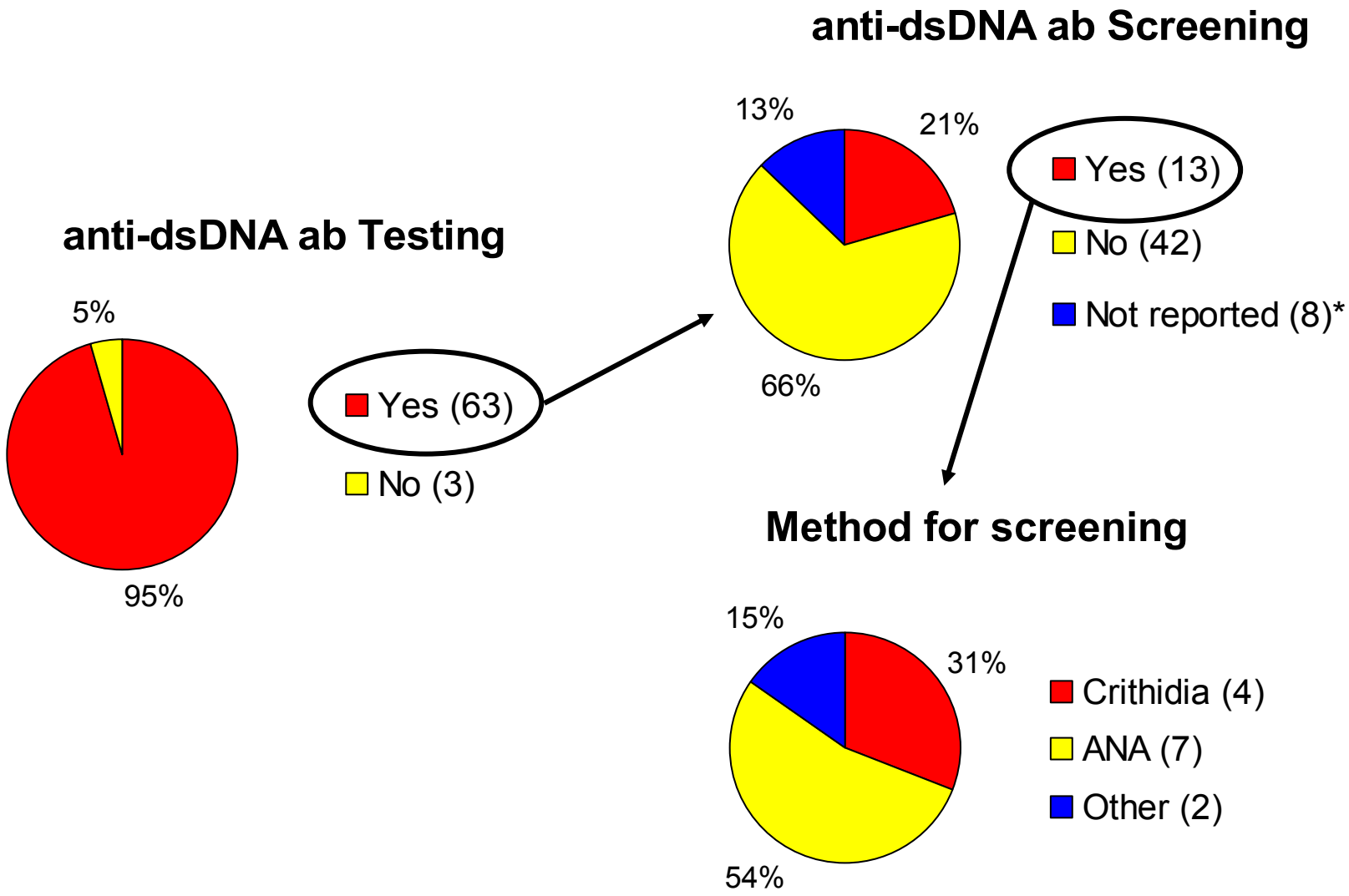
Anti-dsDNA ab testing



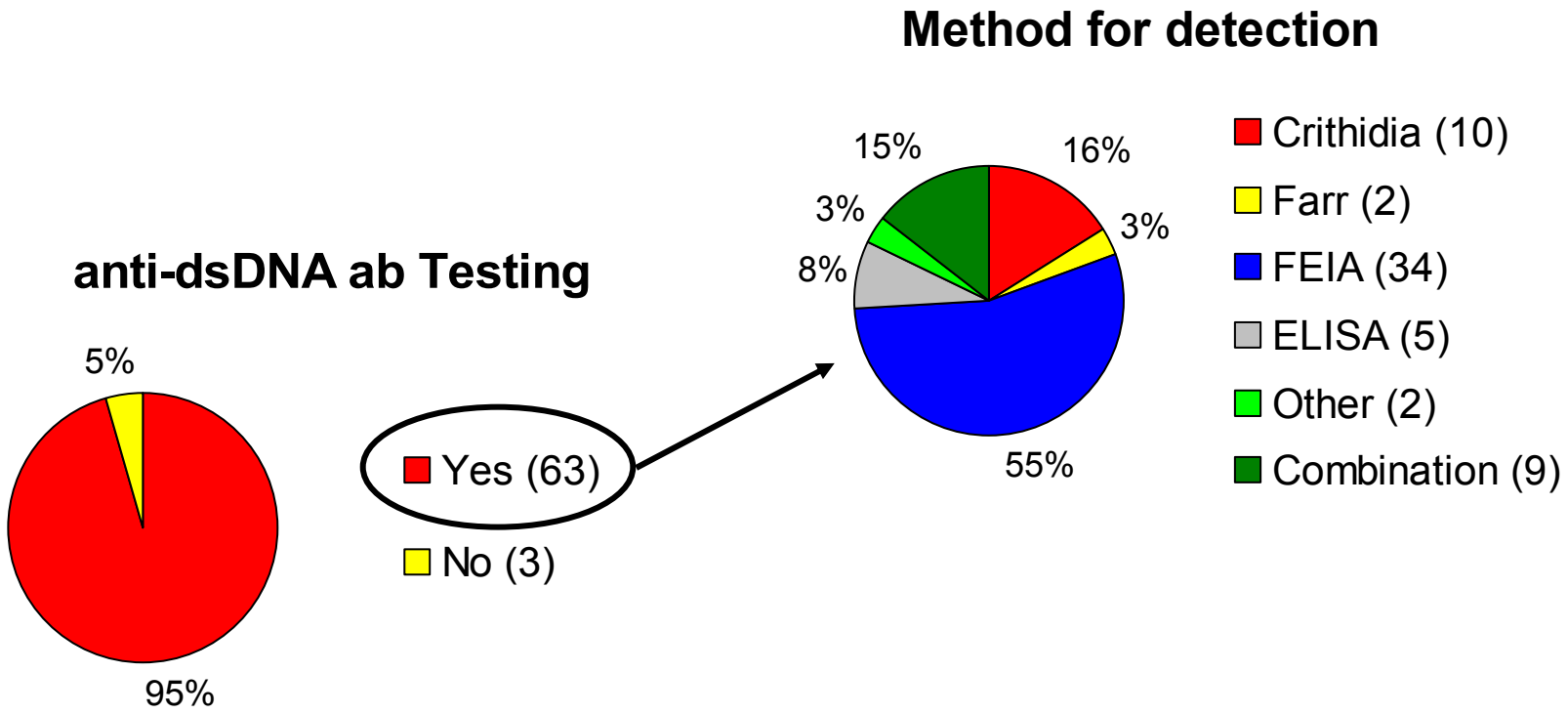
Anti-dsDNA ab screening



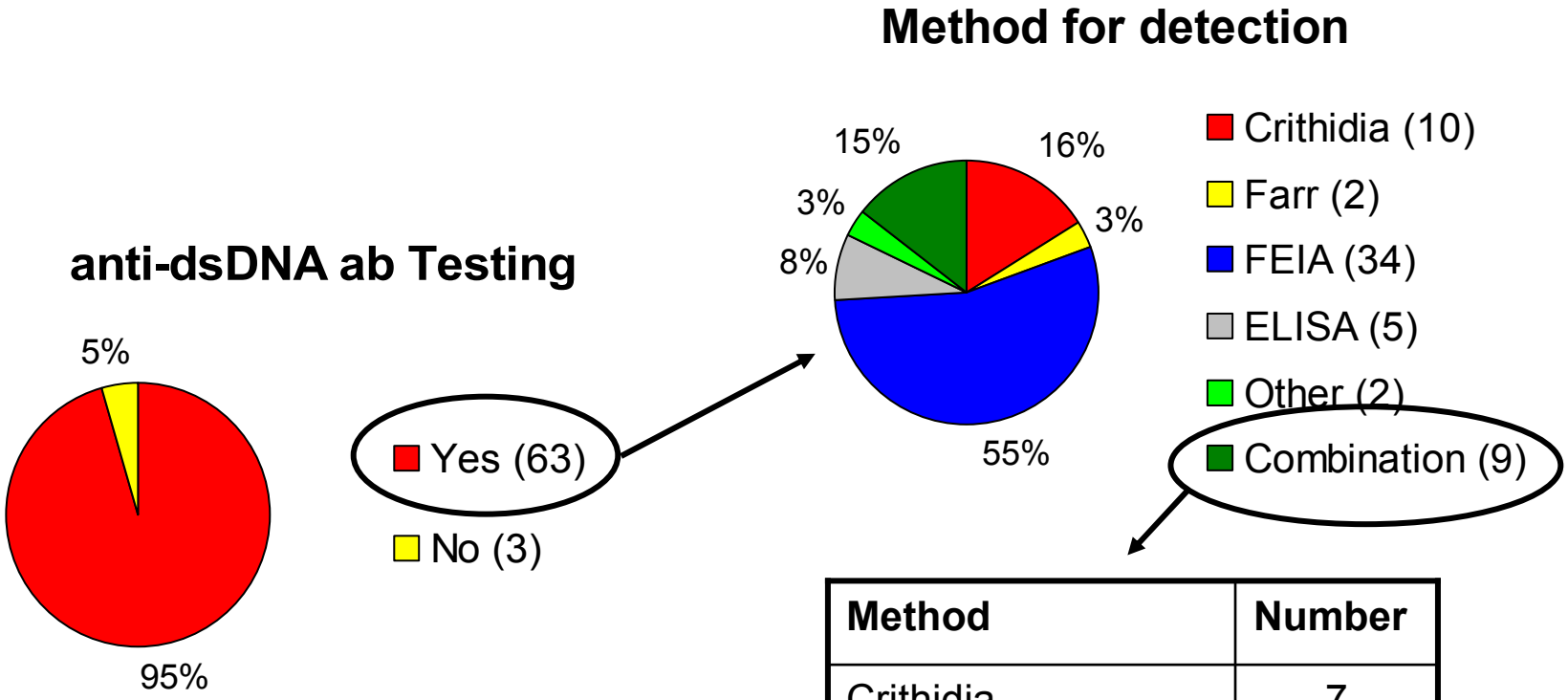
Anti-dsDNA ab screening



Anti-dsDNA ab methods

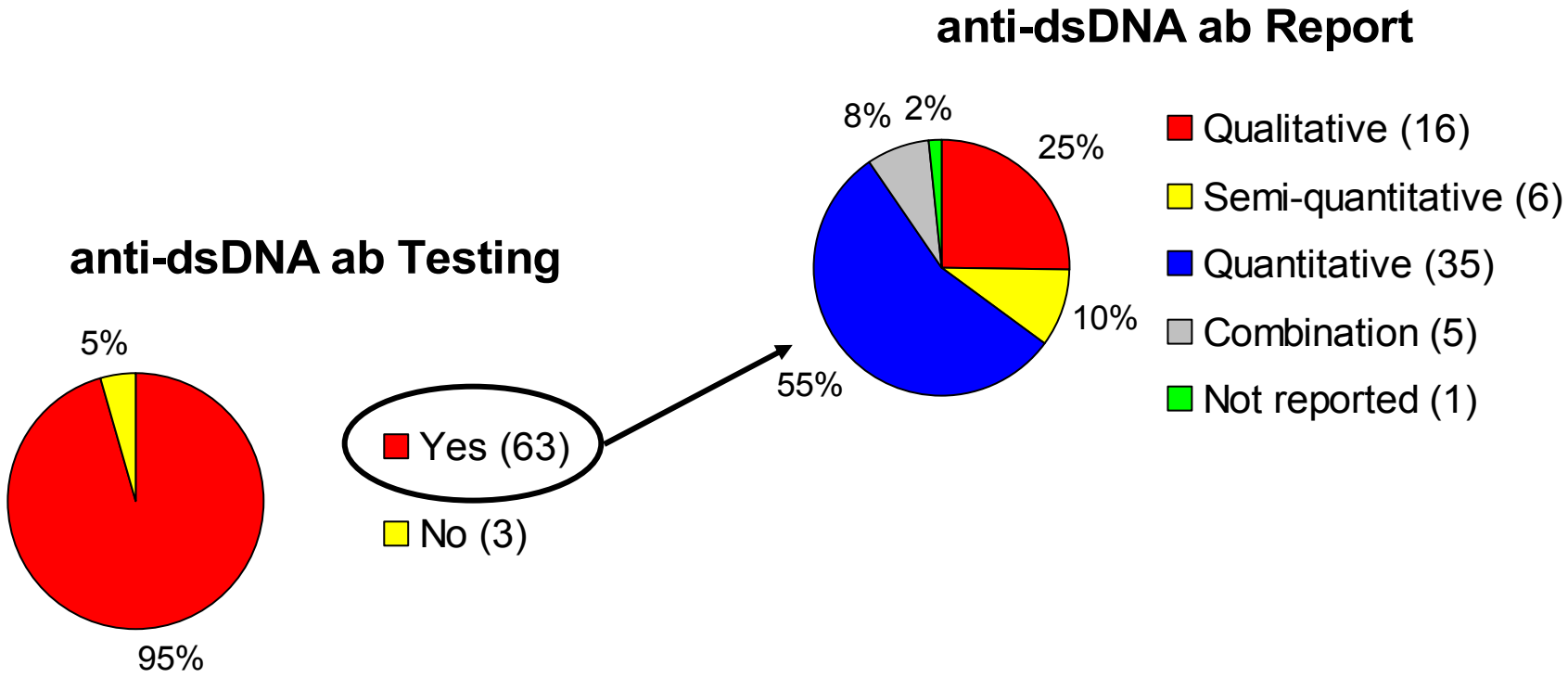


Anti-dsDNA ab methods

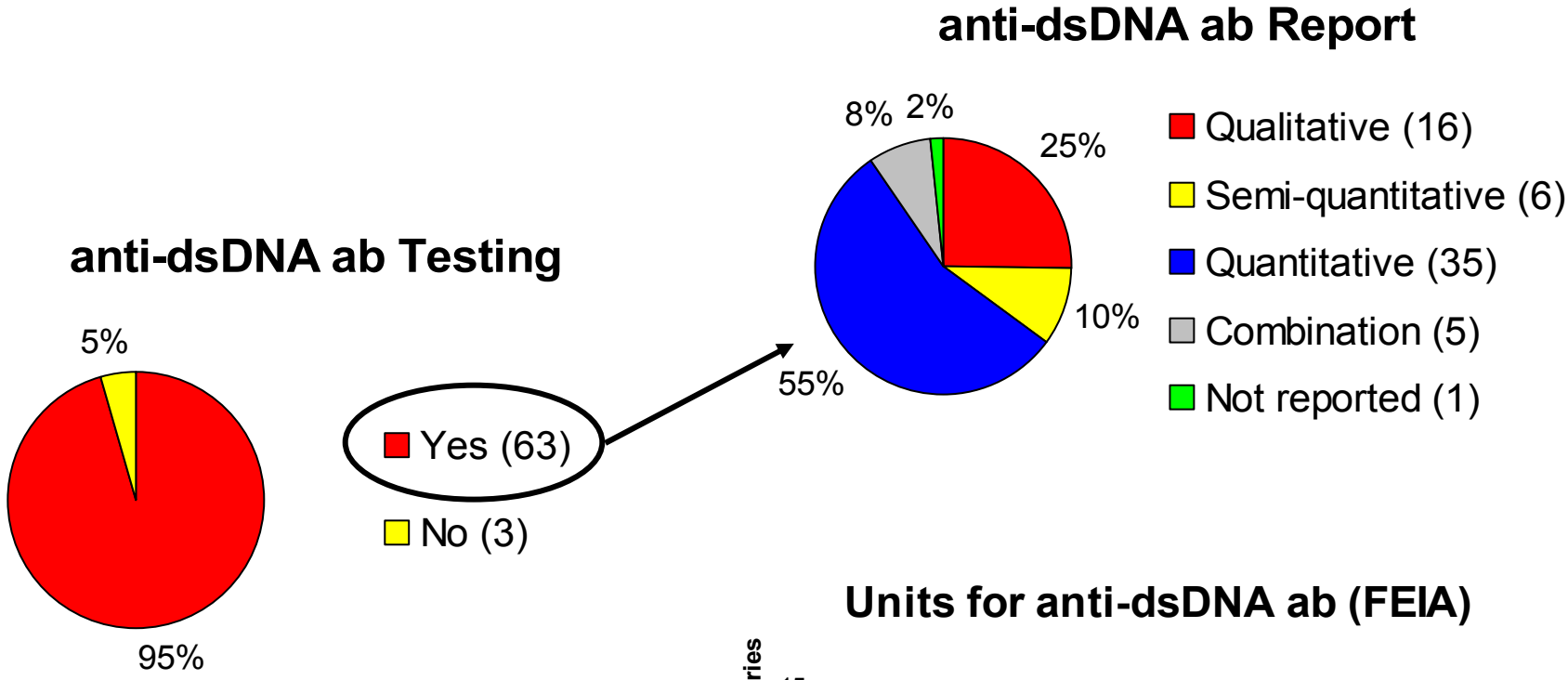


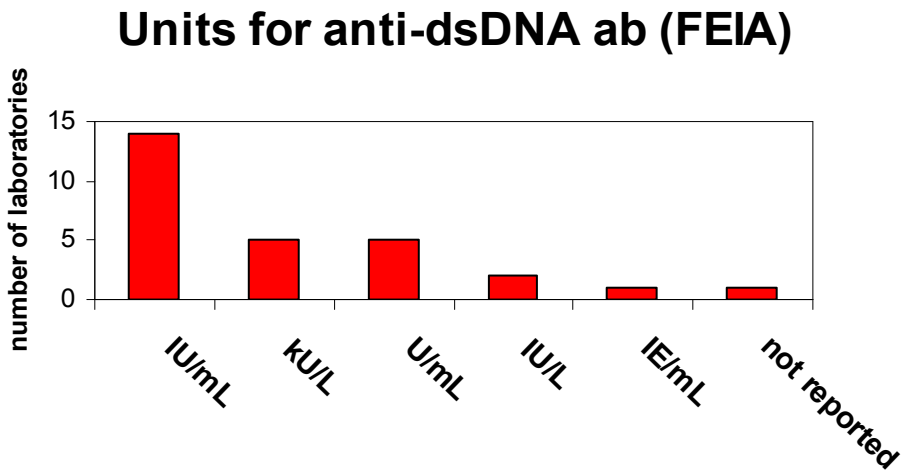
Method	Number
Crithidia	7
Farr	6
FEIA	4
Other	2

Anti-dsDNA ab report



Anti-dsDNA ab report

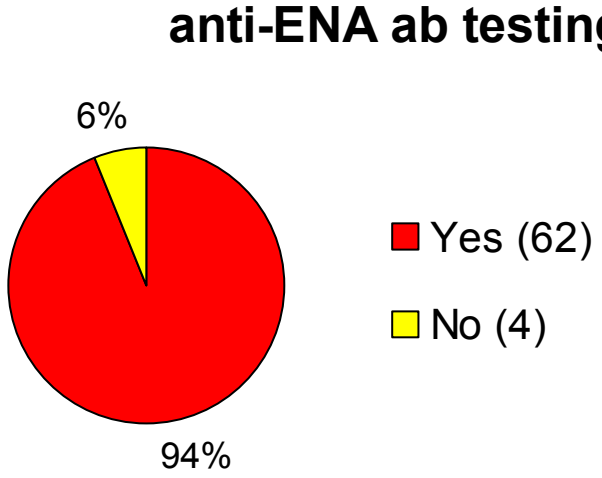




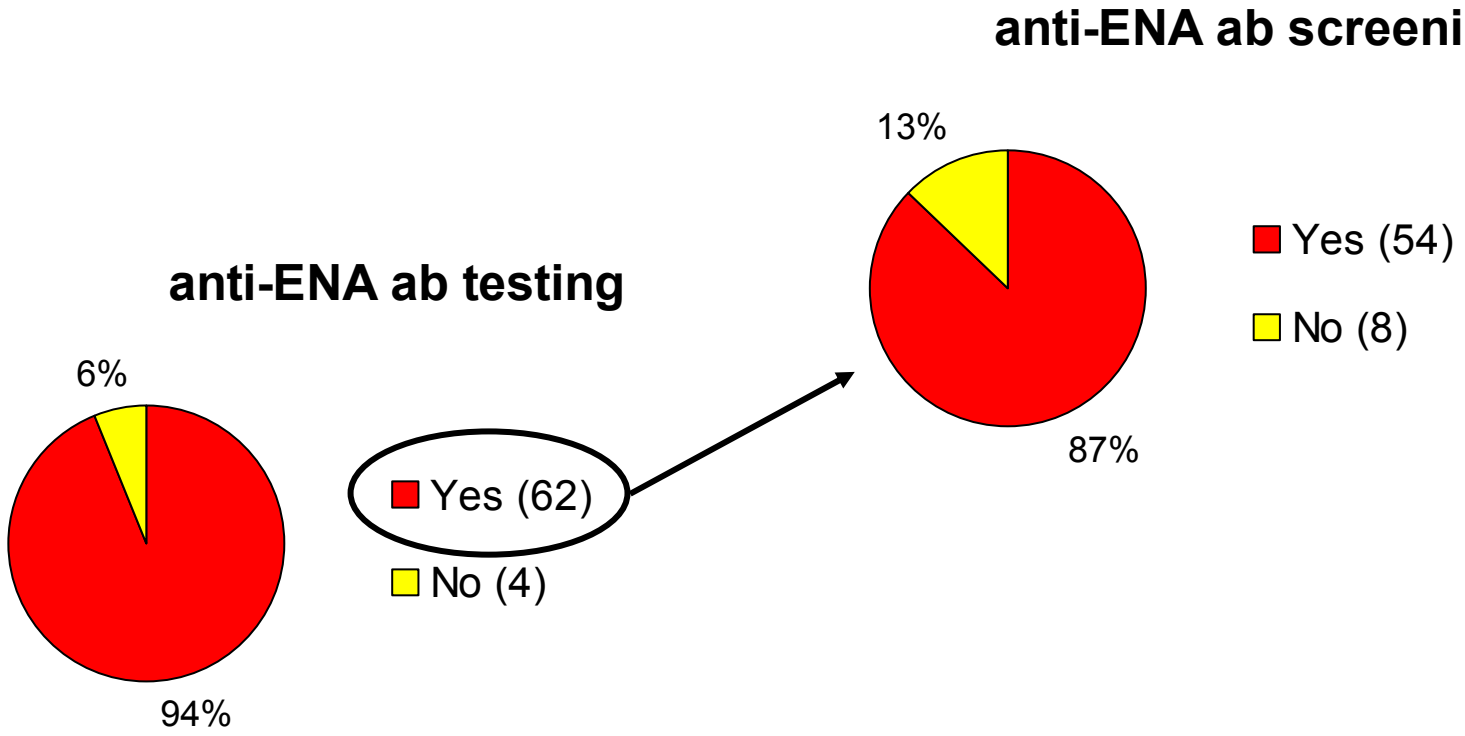
Relation between ANA and anti-dsDNA ab

- 7 labs consider ANA a screening assay for anti-dsDNA ab,
- 11 labs (17%) add ANA if anti-dsDNA ab is requested,
- 11 labs (17%) do not perform anti-dsDNA ab test if ANA is negative,
- 36 labs (55%) add anti-dsDNA ab if ANA is positive,
- 14 of these labs add anti-dsDNA ab only if ANA reveals a homogenous pattern,
- In 19 labs (29%) there seems to be no algorithm for ANA in relation to anti-dsDNA ab.

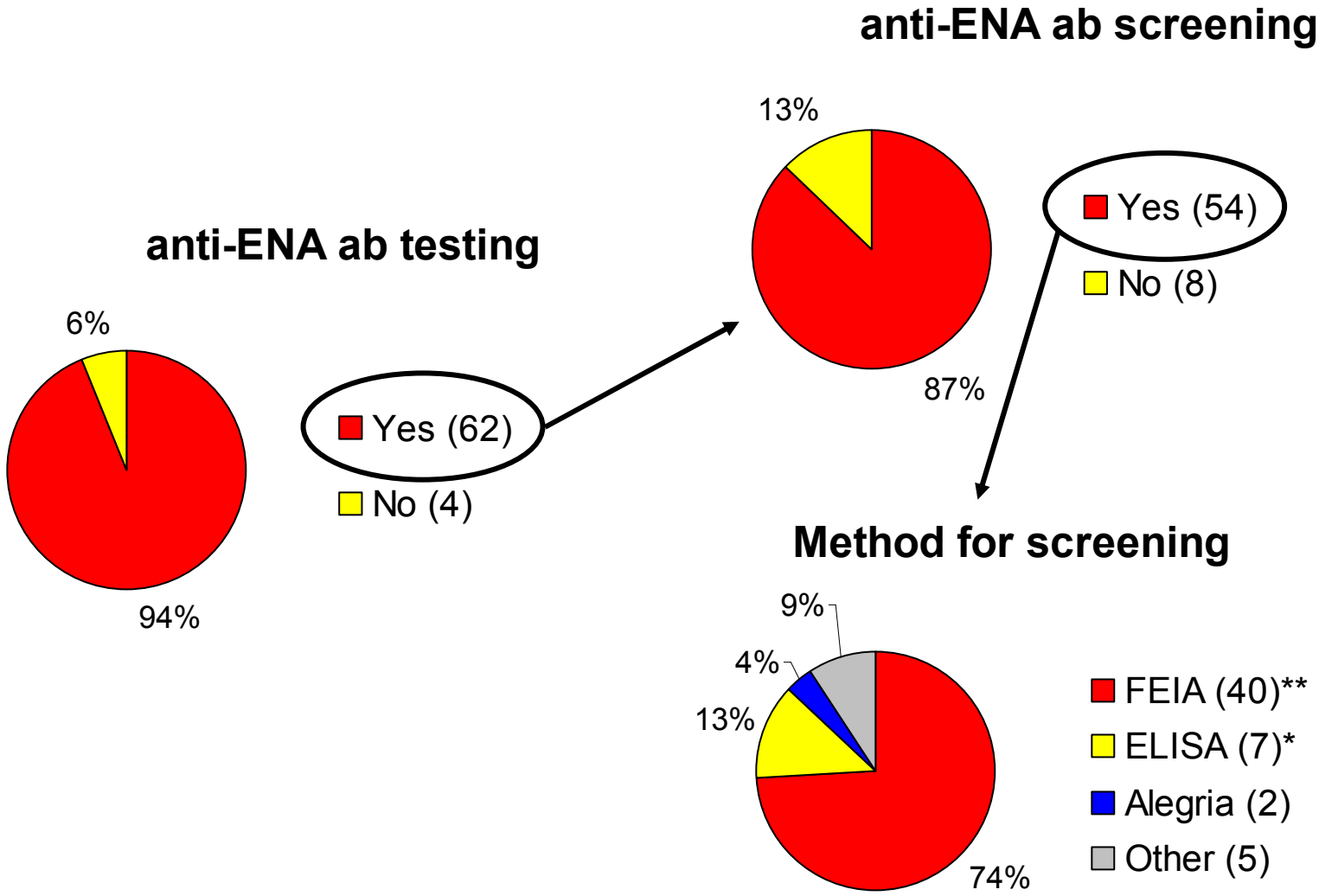
Anti-ENA ab testing



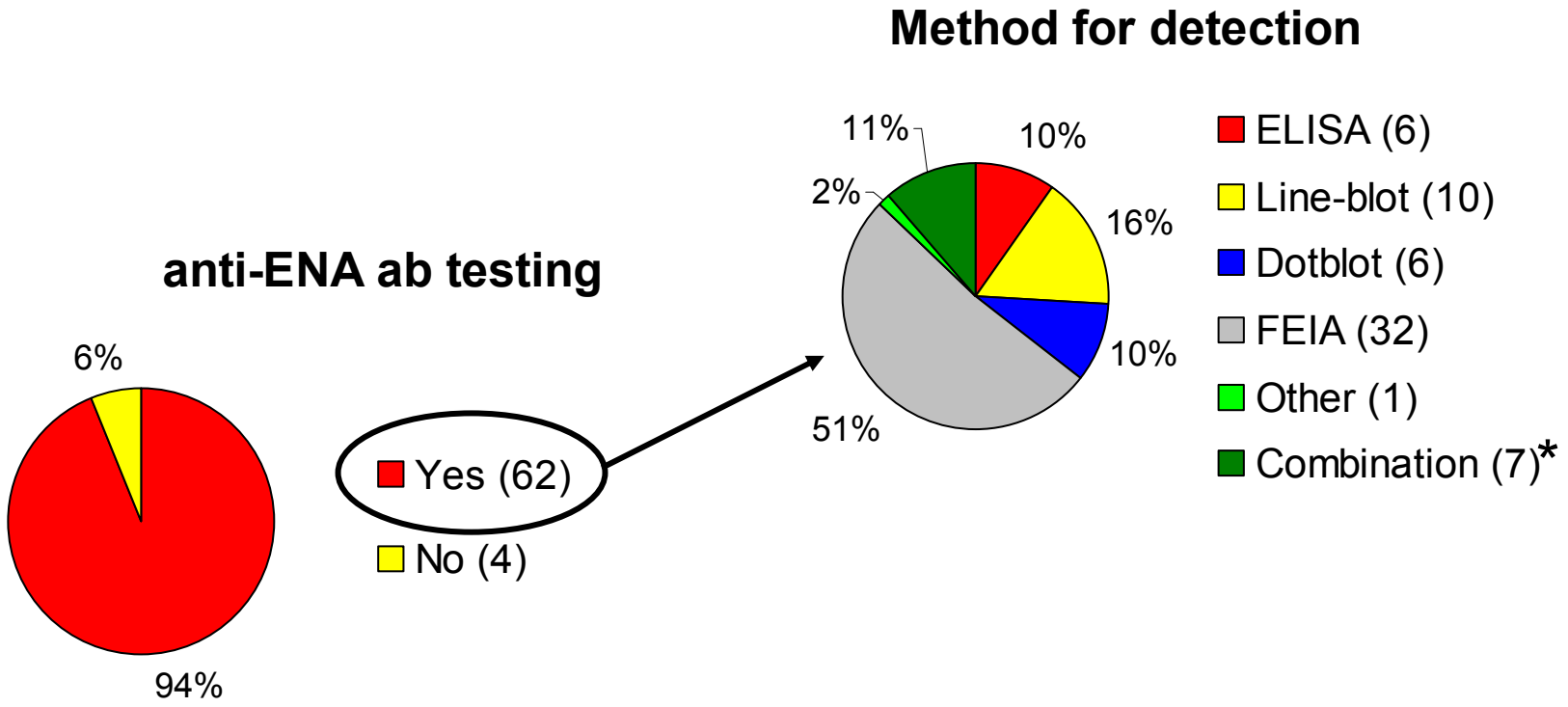
Anti-ENA ab screening



Anti-ENA ab screening

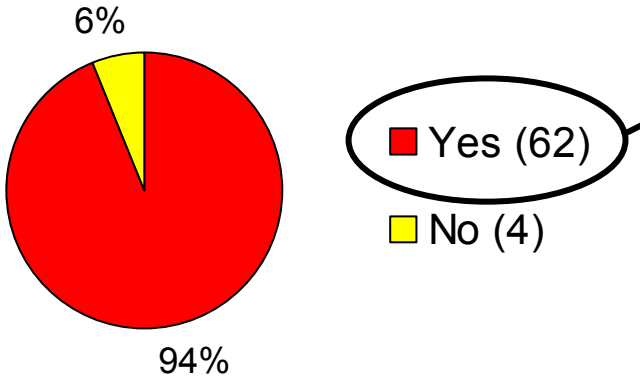


Anti-ENA ab methods

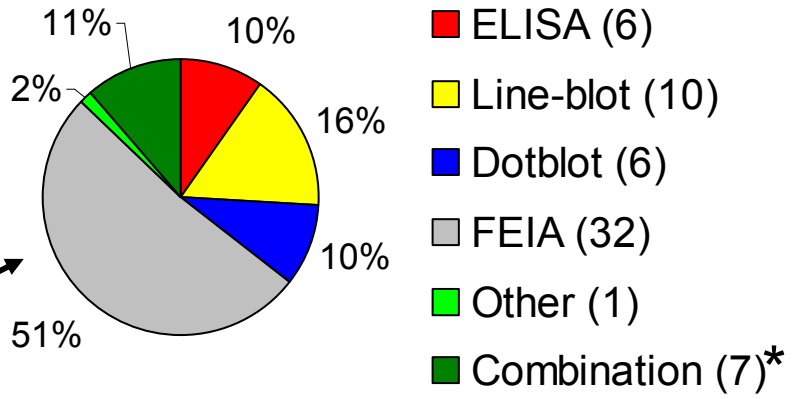


Anti-ENA ab methods

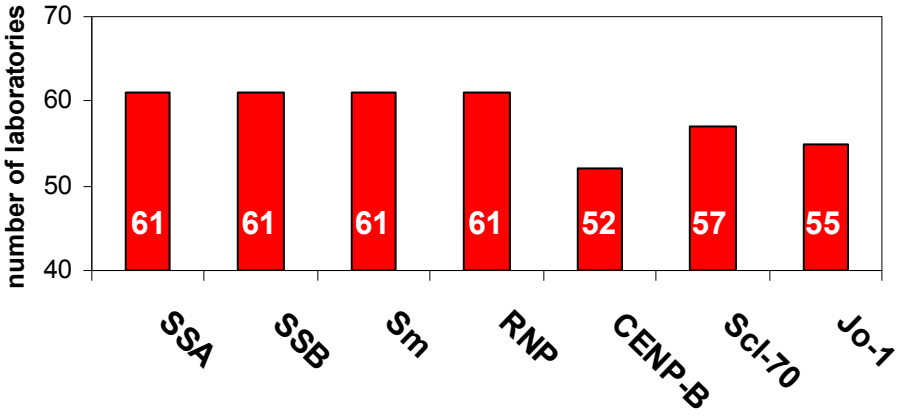
anti-ENA ab testing



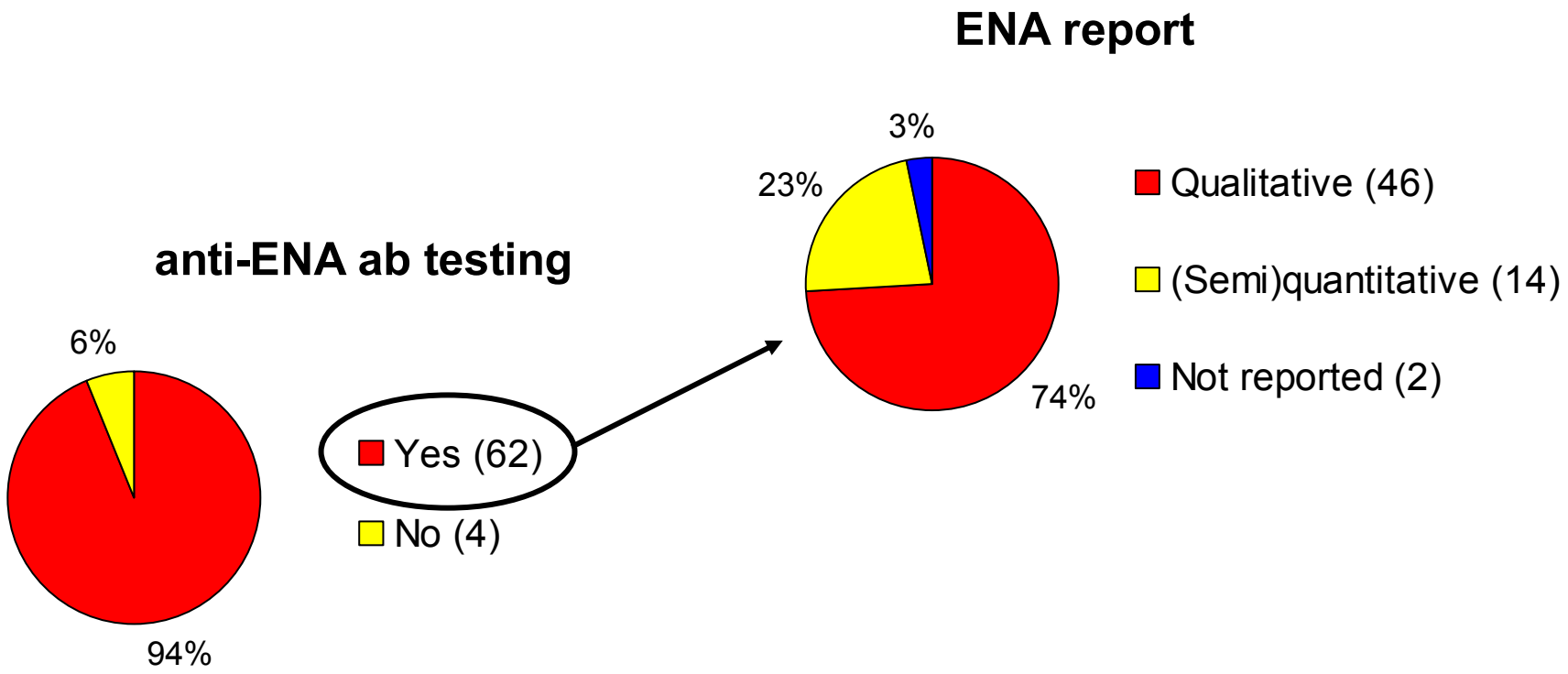
Method for detection



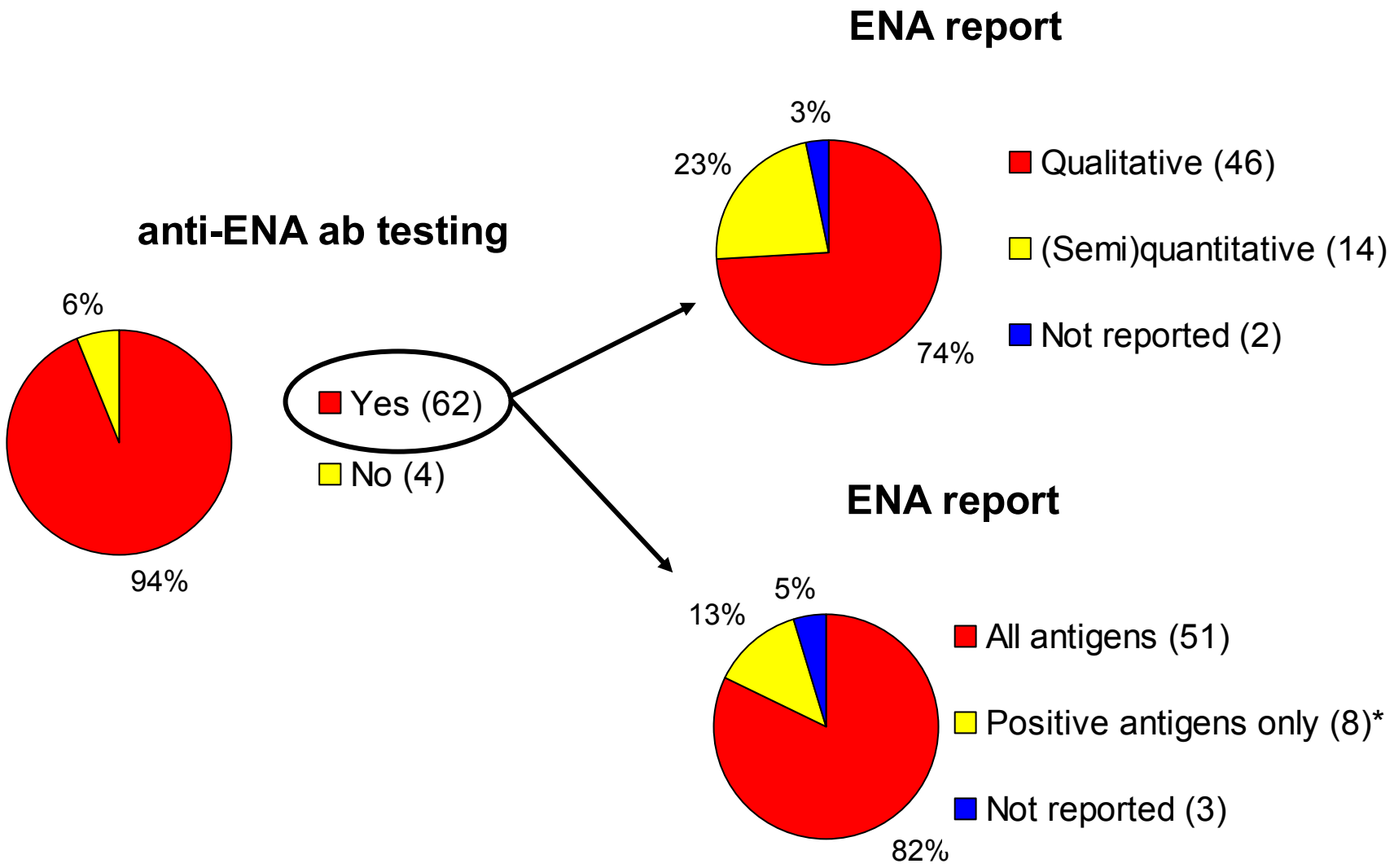
ENA antigen detection



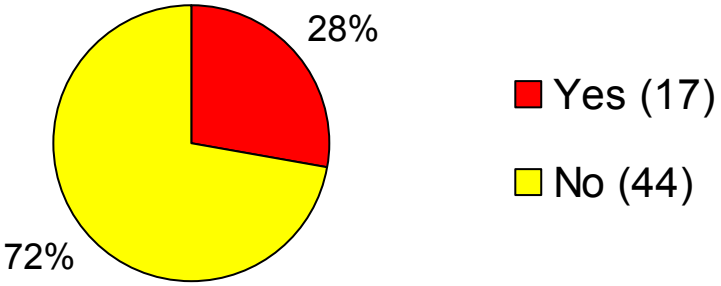
Anti-ENA ab methods



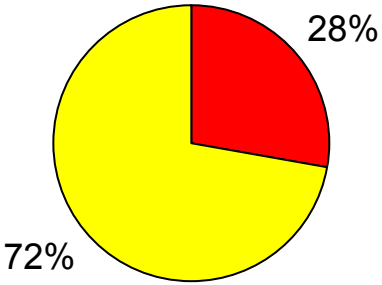
Anti-ENA ab methods

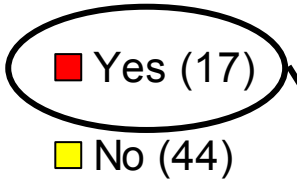


Distinction SSA60 and Ro52

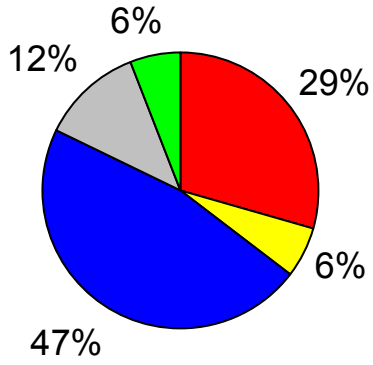


Distinction SSA60 and Ro52



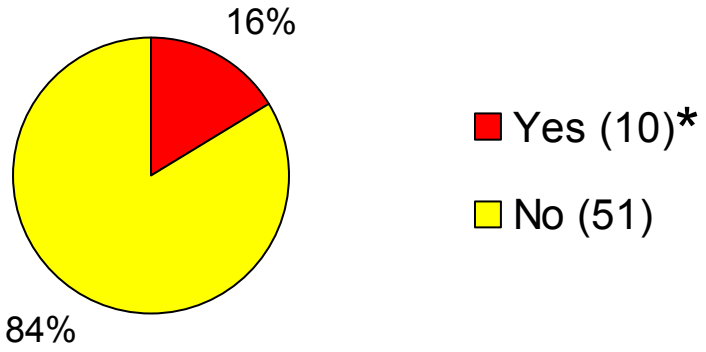


Report of SSA60 and Ro52

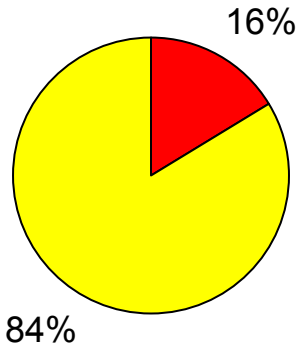


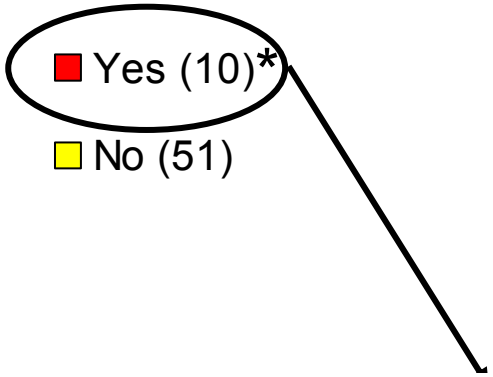
- SSA60+ or Ro52+ = SSA (5)
- SSA60+ = SSA (1)
- SSA60+ = SSA60 / Ro52+ = Ro52 (8)
- Ro52 only if SSA60 is neg (2)
- Other (1)

Distinction SmB and SmD

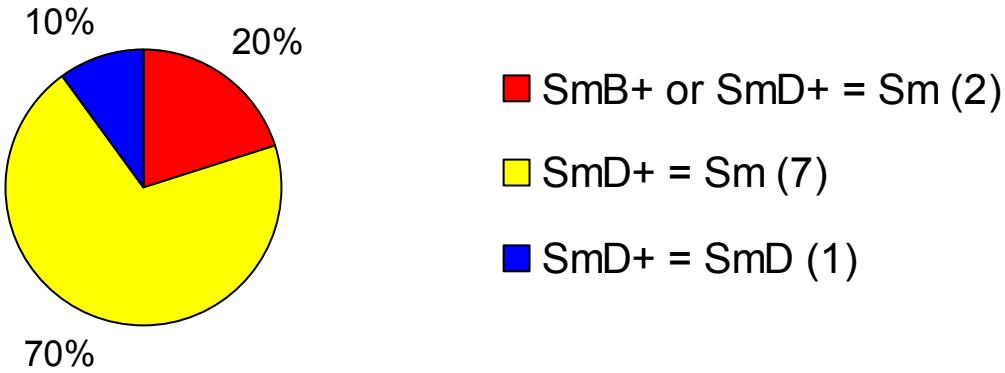


Distinction SmB and SmD





Report of SmB and SmD

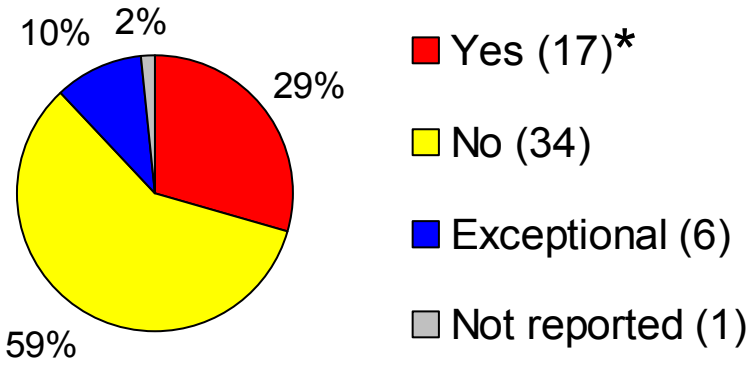


Relation between ANA and anti-ENA ab

- 17 labs (26%) add ANA if anti-ENA ab is requested,
- 21 labs (32%) do not perform anti-ENA ab test if ANA is negative,
- 40 labs (61%) add anti-ENA ab if ANA is positive,
- 7 of these labs add anti-ENA ab only if ANA reveals a specific pattern and/or titer,
- In 14 labs (21%) there seems to be no algorithm for ANA in relation to anti-ENA ab.

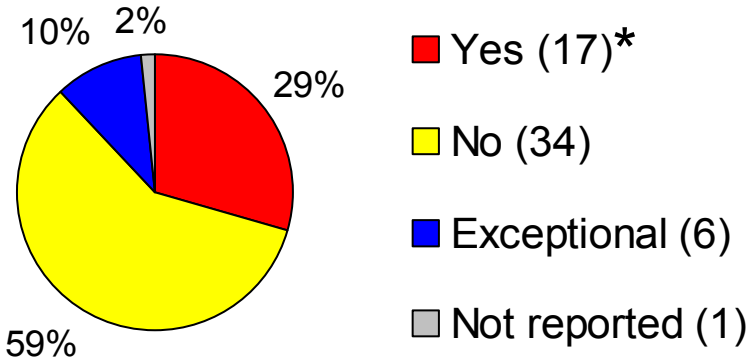
Rapid testing

ANA Rapid test

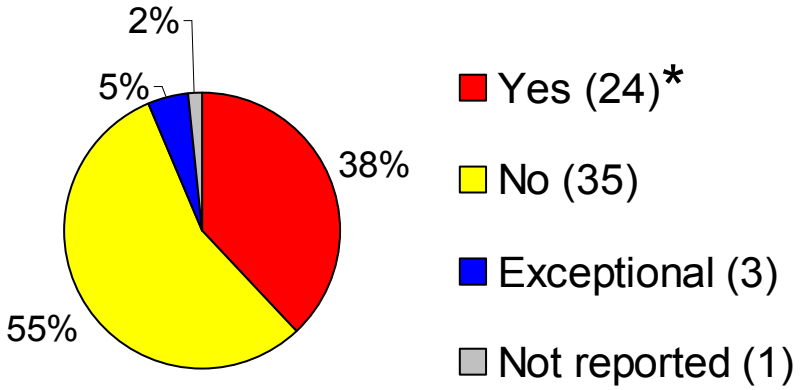


Rapid testing

ANA Rapid test

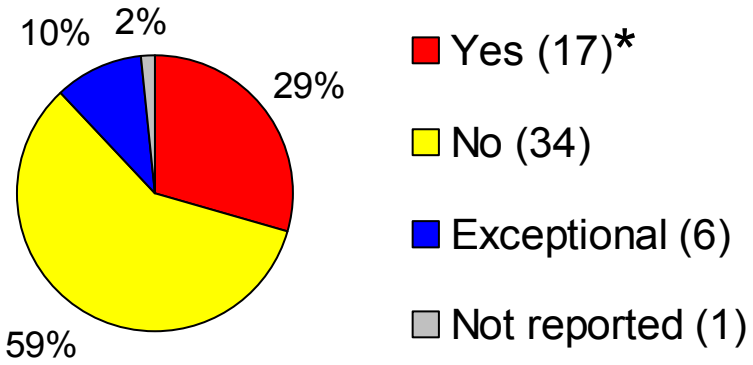


anti-dsDNA ab Rapid test

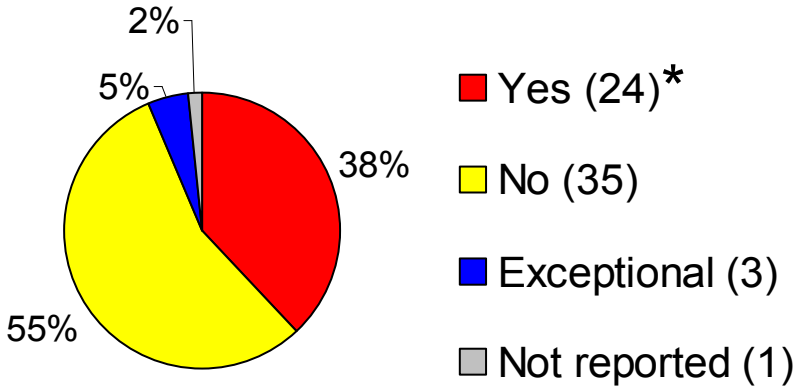


Rapid testing

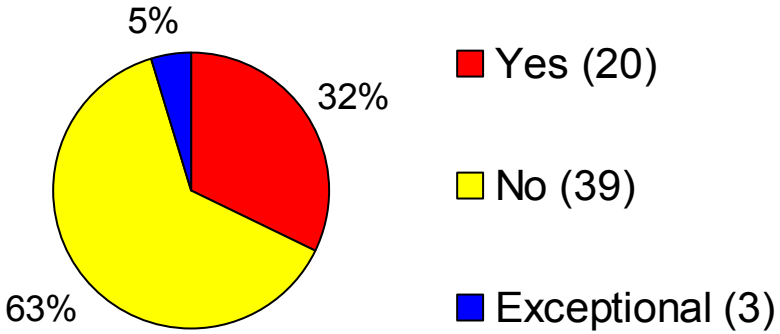
ANA Rapid test



anti-dsDNA ab Rapid test

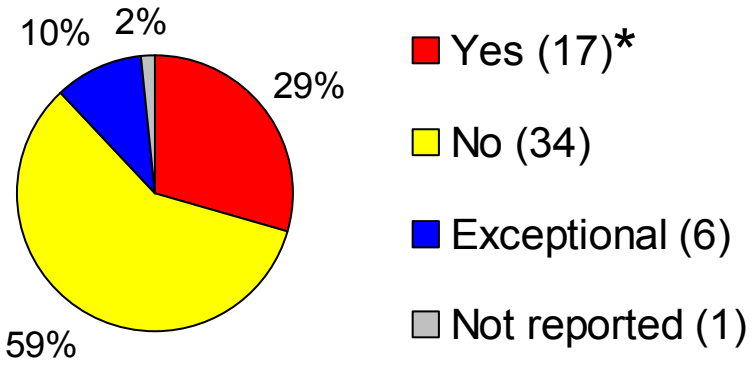


anti-ENA ab Rapid test

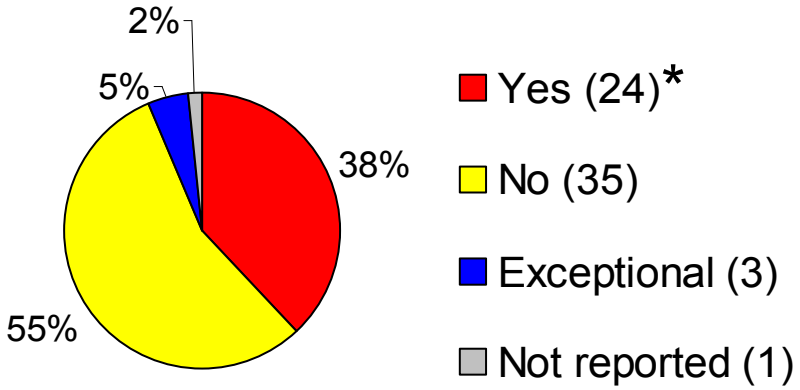


Rapid testing

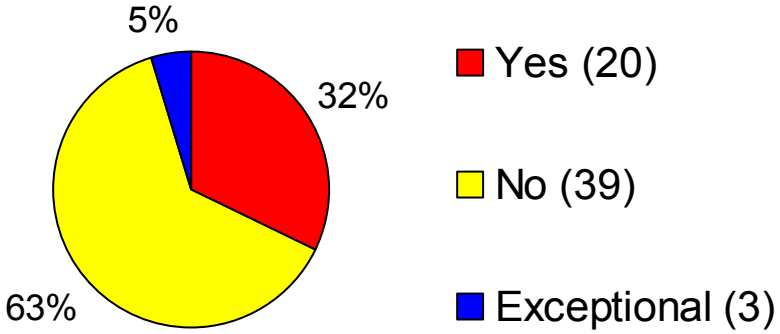
ANA Rapid test



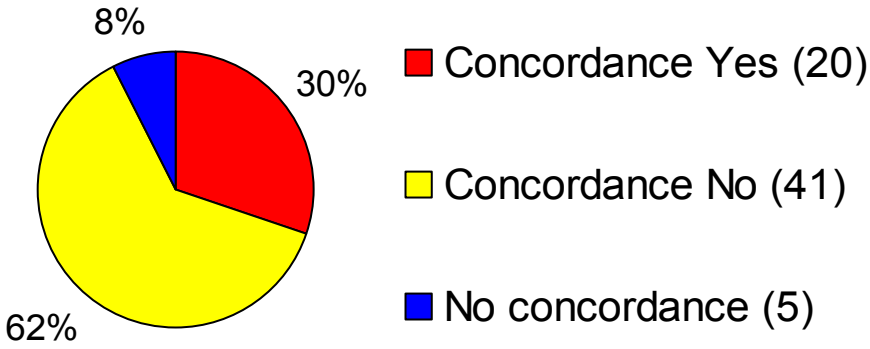
anti-dsDNA ab Rapid test



anti-ENA ab Rapid test



Concordance Rapid testing



Time span for re-testing

n=59*	Diagnosis (n=13; 22%)	Follow-up (n=12; 20%)
ANA	n=8 2.1 months	n=8 3.4 months
Anti-dsDNA ab	n=5 1.7 months	n=4 1.6 months
Anti-ENA ab	n=12 5.8 months	n=10 5.8 months

Major findings

1. ~20% use ELISA/FEIA for ANA testing (n=11),
2. ~40% (IIF) use a start dilution of 1:40 and ~80% of these laboratories do not titrate ANA (n=14),
3. Almost all laboratories (98%) score the ANA pattern; only half of these (53%) report the pattern,
4. ~25% report anti-dsDNA ab only qualitatively (n=16),
5. The relation between a homogenous ANA pattern and anti-dsDNA ab is only poorly translated into a diagnostic algorithm (n=14),

Major findings

6. Only 7 laboratories (11%) use different techniques for anti-ENA ab testing,
7. The majority (74%) reports anti-ENA ab in a qualitative way (n=46),
8. Eight labs (13%) only report positive results for anti-ENA ab,
9. The relation between ANA patterns and/or titers is only poorly translated into a diagnostic algorithm (n=7),

Major findings

10. Many laboratories are not aware of the antigen (SmD) composition of their ENA test system,
11. Allowing rapid testing for non-specific tests, like ANA (n=23) and anti-ENA ab (n=23), is disputable,
12. Allowing rapid testing for anti-dsDNA ab (n=26) should be extended,

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