

Superior detection of syphilis with the rapid test DETERMINE® compared to combined cardiolipin and treponemal specific tests

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Key messages

In our pilot study:

- 1 The rapid DETERMINE® syphilis test is superior to single cardiolipin and dual cardiolipin/treponemal specific tests in syphilis diagnosis.
- 2 Although rapid immunoassays are not recommended in European clinical guidelines, this study shows that DETERMINE® syphilis test provides results similar to those of laboratory based IgM & IgG analysis.
- 3 Underdiagnosis of syphilis may be commonplace in Spain since IgG and IgM based tests are not routinely performed.

Methods & materials

1898 consecutive patients with no prior history of syphilis were tested between 2007 and 2010 with or without clinical signs or symptoms of syphilis.

Serum (if available) or finger prick samples with EDTA tubes were used to perform the DETERMINE® TP test (Alere Healthcare) following manufacturer's instructions. The results were read by a laboratory technician and the attending physician.

All positive results

- Were confirmed with a laboratory analysis of RPR (or VDRL) and FTA
- Signs & symptoms, history of contact with syphilis, HIV status and clinical response to single IM benzathine penicillin 2.4 MU noted.

True positives defined as sustained positive result with DETERMINE® at 7 day follow-up plus:

- Positive cardiolipin and/or specific treponemal positive results or
- Classical signs and symptoms of syphilis which resolved completely with single dose benzathine penicillin or
- Positive cardiolipin and/or specific treponemal positive results at follow-up

False positives defined as:

- Negative cardiolipin and specific treponemal positive tests at baseline and at 7 days follow-up. Measurement of direct IgG or IgM by ELISA was not possible in this study due to financial constraints

Introduction

Most national European guidelines regarding syphilis testing advocate the use of IgM and IgG specific tests, due to their high specificity and sensitivity compared to specific treponemal and cardiolipin tests.^[1-3]

Currently these guidelines do not recommend the use of rapid test kits as clinical tools for lack of clinical evidence despite their being both specific antibody and point-of-care tests.

False negative cardiolipin test results on undiluted serum have been reported in secondary and early latent syphilis due to the prozone phenomenon, and which has been seen to be more common in patients with HIV infection.^[4-8]

In our Primary Care centre we have routinely used the DETERMINE® syphilis TP test (Alere Healthcare) in whole blood finger-prick samples as our screening and diagnostic tool for syphilis in nearly 2000 samples since 2007. The manufacturer has found specificity of 100% and sensitivity of around 92% in whole blood and up to 98% in serum.^[9] This is supported by published data by Diaz T et al^[10], but no clinical advantage was apparent in the DETERMINE® system in the just one publication in a clinical setting. However, the study design of Campos et al was questionable as whole blood used should have been heparinised and doubtfully relevant comparators were employed.^[11]

In this poster we review the DETERMINE® test in a Primary Care centre to quantify its performance in diagnosis versus other syphilis tests in a natural setting, that is to say, with fingerprick whole blood if no other serology was performed at the same time, comparing results with combined treponemal specific and cardiolipin tests (which remain the standard in Spain).

Results

The attending physician and laboratory technician concurred on 100% of positive and negative results. Of the 107 cases being positive in DETERMINE®, treponemal tests confirmed 87 of them, cardiolipin tests were also positive in just 73 tests. 20 cases were negative for both treponemal and cardiolipin tests (Chart 1).

CHART 1
All positive DETERMINE® tests Total 107 cases

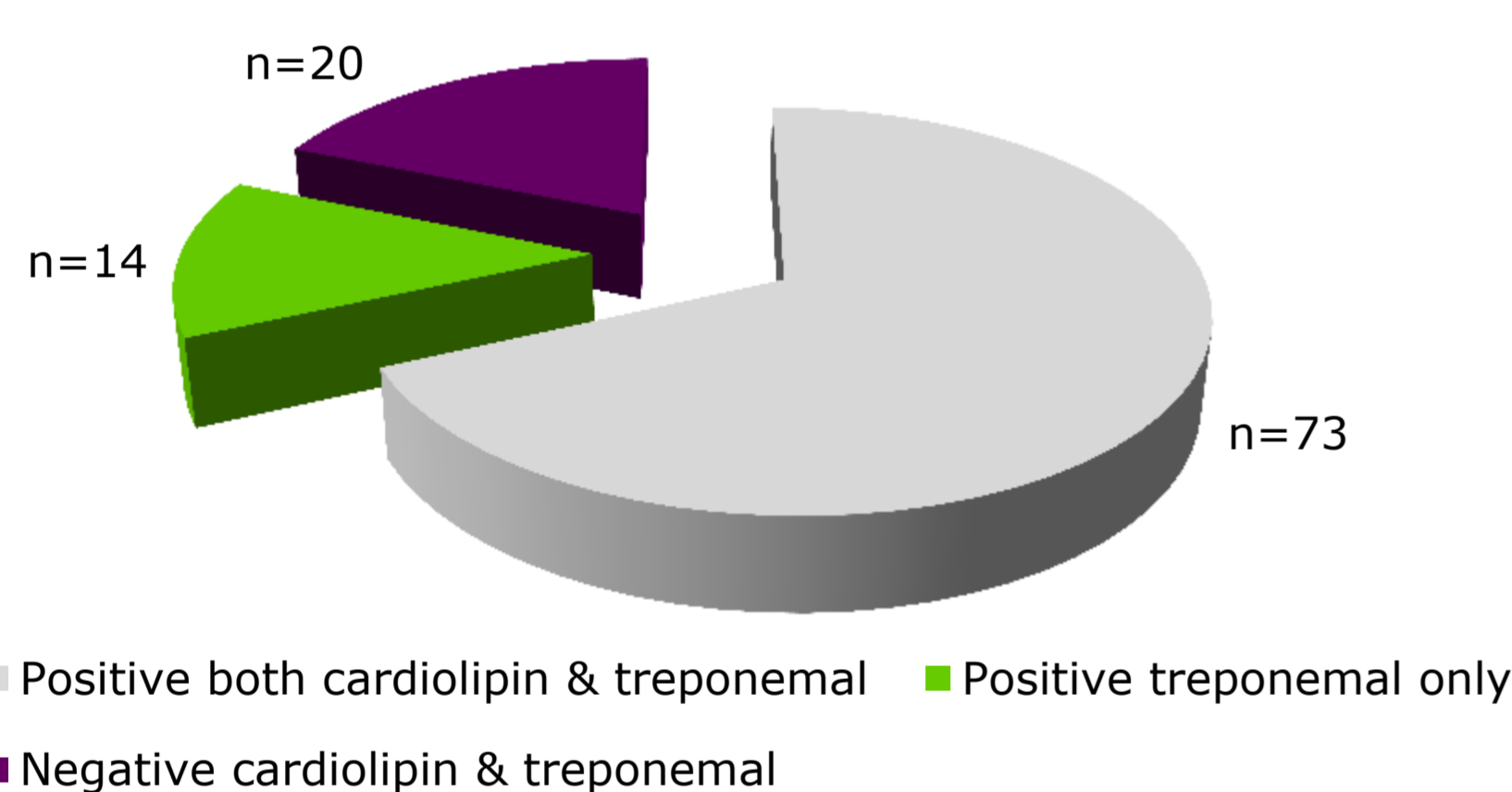
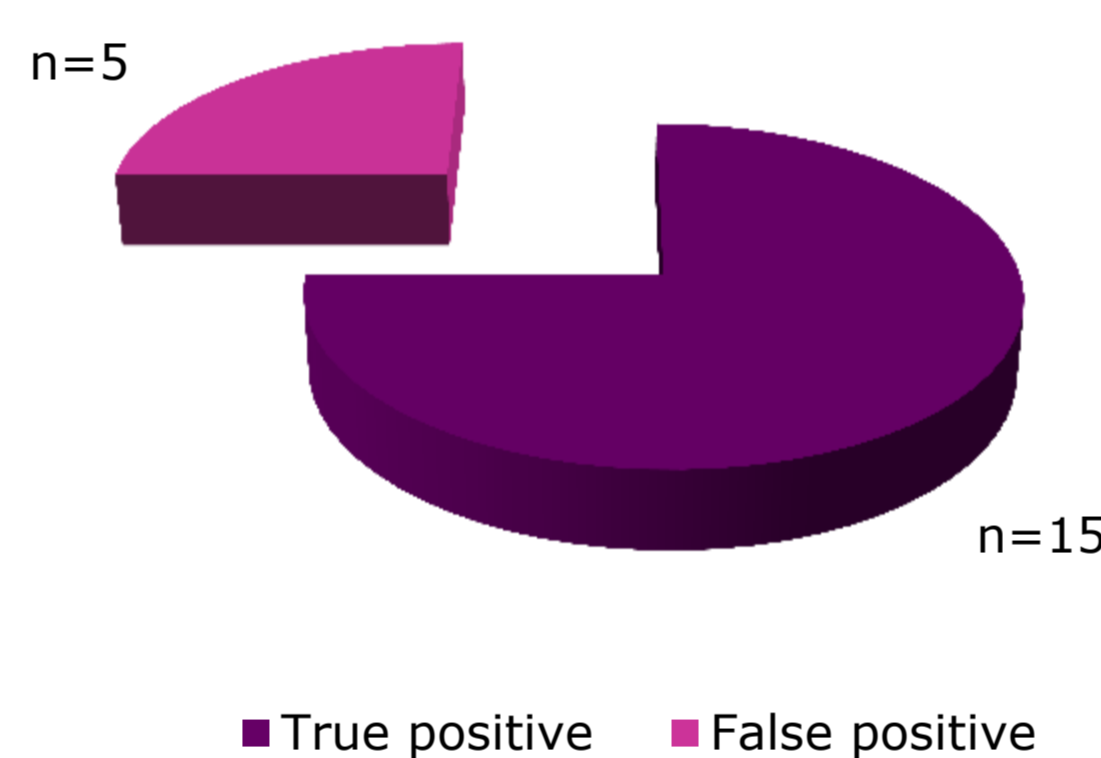
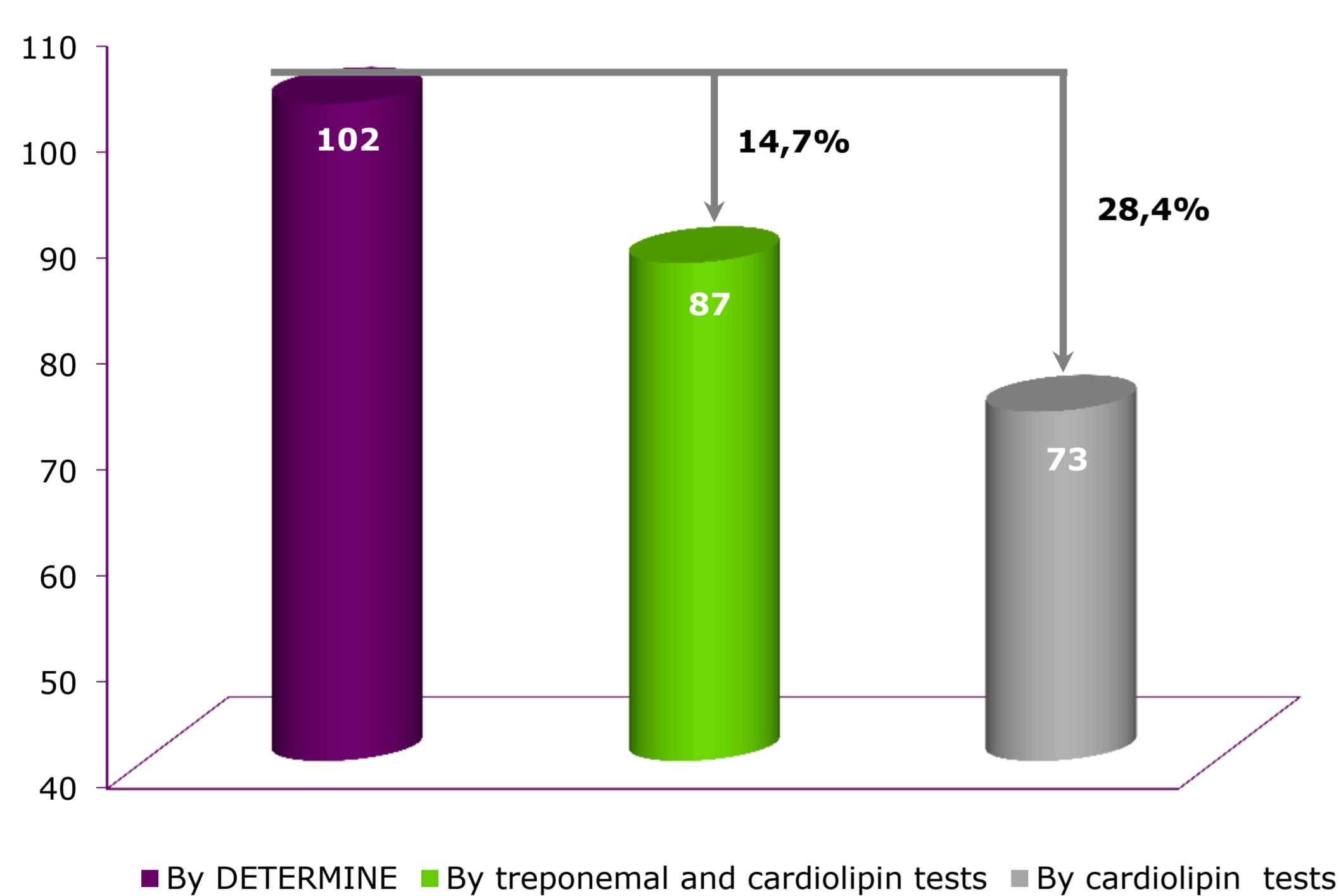


CHART 2
Positive DETERMINE® tests & dual negative cardiolipin & treponemal tests Total 20 cases



Of the twenty cases positive in DETERMINE® and negative in both treponemal and cardiolipin tests, 15 were considered true positive results for by fulfilling the aforementioned criteria (Chart 2) These 15 cases are profiled briefly in Table 1.

CHART 3
Detection of syphilis (cases) – overall comparison



A positive cardiolipin result was always accompanied by a positive treponemal result. In those cases where cardiolipin tests were positive the DETERMINE® test detected 28,5% more cases. In cases where only treponemal tests were positive, DETERMINE® detected 14,7% more cases (Chart 3).

The 5 cases considered false positive results could not be confirmed with any further tests (such as IgG and IgM by ELISA) due to financial constraints.

Given that these 5 false positives were seen in the context of 1898 tests, the overall rate of false positives was 0,26% of all clinical samples for DETERMINE®.

Discussion & conclusions

Our results refute the findings of Campos et al^[11] and show better results than Diaz et al.^[10]

We believe that superiority may be explained simply by direct detection of early IgM antibody. Also, this test is not susceptible to the prozone phenomenon.

In Spain, the primary care public health sector does not routinely perform specific IgG and IgM tests for syphilis diagnosis. In fact it is common practice in STI centres in Madrid to only use single cardiolipin tests, not combinations. Our study suggests that more than a quarter of all cases could go undiagnosed in these centres.

In our study approximately one in every 400 tests performed was a false positive. However, it is worthy of note that in 4 of these 5 patients there was a history of contact with confirmed cases of syphilis. Due to financial constraints we were unable to perform IgM/IgG tests by ELISA as definitive confirmation. Since performing this study, we have detected IgM and IgG positive in all but one case where DETERMINE® positives were not confirmed by dual conventional tests making false positives even less common.

Table 1 Cases with criteria for positivity:

	Clinical signs and symptoms	HIV	Criterion for positivity
A	Small but deep ulcer on foreskin two weeks after sexual contact with confirmed secondary syphilis	NEG	Rapid resolution of symptoms following treatment with single dose penicillin*
B	Genital ulceration with classical signs of chancre	NEG	RPR positive within 1 week of treatment with single dose penicillin*
C	None	NEG	VDRL positive within 1 week of treatment with first dose penicillin*
D	Genital ulceration with classical signs of chancre	NEG	RPR positive within 1 week of treatment with single dose penicillin*
E	None (sexual contact with confirmed syphilis)	NEG	RPR positive within 1 week of treatment with single dose penicillin*
F	Generalised maculopapular rash with constitutional symptoms	NEG	Rapid resolution of symptoms following treatment with single dose penicillin* and positive RPR (in other centre) within 1 month of treatment
G	Rectal discharge	POS	RPR and VDRL positive within 1 week of treatment with single dose penicillin*
H	Genital ulceration with classical signs of chancre. Recent contact with primary syphilis	NEG	Rapid resolution of symptoms following treatment with single dose penicillin*
I	Genital ulceration with classical signs of chancre	NEG	Rapid resolution of symptoms following treatment with single dose penicillin*
J	Maculopapular rash of head and neck with inguinal adenopathy	NEG	Jarisch-Herxheimer reaction and rapid resolution of symptoms following treatment with single dose penicillin*
K	None	NEG	TPHA in other centre positive within 1 week of treatment with first dose penicillin*
L	Genital ulceration with classical signs of perianal chancre	POS	Rapid resolution of symptoms following treatment with single dose penicillin* and positive RPR within 1 week of treatment
M	Genital ulceration with classical signs of chancre. Recent contact with primary syphilis	NEG	Rapid resolution of symptoms following treatment with single dose penicillin*
N	Superficial & generalized painless ulceration on mouth and perianal area. Contact confirmed with secondary syphilis	NEG	Rapid resolution of symptoms following treatment with single dose penicillin*
O	Generalised maculopapular rash with palmar lesions	NEG	RPR and FTA-Abs positive within 1 week of treatment with single dose penicillin*

* Benzathine penicillin G 2.4 MU by intramuscular injection

The DETERMINE® Syphilis TP test provides a simple, rapid and precise tool in the prompt diagnosis and treatment of syphilis in primary care and appears to be superior to cardiolipin and treponemal tests.

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