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Title: Recall of symptoms and treatment of syphilis and yaws by healthy blood donors screening positive for syphilis in Kumasi, Ghana

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1 **Recall of symptoms and treatment of syphilis and yaws by healthy blood** 2 **donors screening positive for syphilis in Kumasi, Ghana**

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10 ***Abstract***

11 **Objective:** To describe the recalled medical history, clinical manifestations and treatment of yaws and
12 syphilis by syphilis sero-reactive blood donors in Kumasi, Ghana

14 **Methods:** Of the 526 sero-reactive blood donors tested with syphilis rapid diagnostic test (RDT) and later
15 with rapid plasma reagin (RPR) from Komfo Anokye Teaching Hospital, Kumasi, Ghana, 471(89.5%) of
16 them who were confirmed with Ortho-Vitros® Syphilis TP test as the gold standard were
17 interviewed to determine past or present clinical manifestations of yaws and syphilis.

19 **Results:** Of the 471 respondents, 28 (5.9%) donors gave a history of skin lesions and sores and of these,
20 four (14.3%) who were all males and RPR positive, recalled a diagnosis of syphilis. All four reported
21 having had skin lesions/bumps with slow healing sores but only one of them had these symptoms before
22 the age of 15.

24 **Conclusions:** A small proportion of confirmed sero-reactive donors in our sample had any recall of
25 symptoms or treatment for yaws or syphilis. Our data suggest that clinical questioning adds little further
26 information to the current screening algorithm. The relative contribution of yaws and syphilis to frequent
27 positive tests in endemic areas remains speculative.

29 **Background**

30 Yaws is a neglected non-venereal endemic treponematosi s caused by the bacterium *Treponema*
31 *pallidum* subspecies *pertenue*¹. It is spread by direct skin-to-skin contact predominantly
32 affecting children less than 15 years of age living in poor socioeconomic conditions in certain
33 rural, wet, tropical areas². In Ghana, a total of 28,000 cases were reported in 2008 and 25, 000 in
34 2010. In 2012, WHO launched a new initiative to eradicate yaws globally by 2020³ using the
35 Morges strategy. The clinical manifestations of yaws include multiple papillomas, non-tender
36 ulcers, sores, plantar hyperkeratosis and pigmentation of the palms and soles, followed by
37 gummata in the last stage¹.

38 Syphilis is a sexually transmitted disease caused by *Treponema pallidum* subspecies *pallidum*. It
39 can also be transmitted via blood transfusion although the actual risk is low⁴. Syphilis starts with
40 primary lesion (chancre - usually on the genitals) followed by a polymorphic rash and
41 lymphadenopathy. This is followed by the occurrence of generalized condition with
42 parenchymal, systemic, and mucocutaneous manifestations⁵. The end result may include
43 dementia, gummata, blindness, paralysis, or death.

44 Usually yaws and syphilis can only be distinguished by epidemiological characteristics and
45 clinical manifestations as the commonly used antibody tests cannot discriminate one disease
46 from the other⁶.

47 This paper reports on recalled history of clinical manifestations of yaws and syphilis by syphilis
48 sero-reactive blood donors in Kumasi, Ghana.

49

50 **Methods**

51 Of the total of 16016 blood donors, tested with a treponemal Fortress rapid test (Fortress
52 Diagnostics Limited, Antrim – UK) to *T. pallidum* in serum or plasma antibodies (IgG and IgM),
53 526 (3.3%) were sero-reactive to syphilis. These were further tested with rapid plasma reagin
54 (RPR, BD Macro-VueTM Card test – New Jersey, USA) to detect potential active infections. Out
55 of these, 478 were confirmed with Ortho-Vitros® Syphilis TP test as the gold standard. Of these,
56 471 confirmed syphilis sero-reactive blood donors (a response rate of 98.5%) were interviewed
57 to determine past or present clinical manifestations of yaws and syphilis (figure 1). Subjects were
58 interviewed by a laboratory scientist with semi-structured questionnaire in local dialect for the
59 presence or absence of current or previous sores or skin ulcers, skin lesions/bumps on the face,

60 hands, feet, and genitals. They were additionally asked about slow healing sores and at what age
61 they experienced symptoms. They were also asked about any treatment given at the time of these
62 symptoms.

63 Data were recorded on an Excel spreadsheet and exported into STATA (STATA CORP, Texas,
64 version 12.0) for analysis. We obtained approval for this study from the ethics committees of
65 Kwame Nkrumah University of Science and Technology (KNUST) Kumasi, Ghana, and
66 Liverpool School of Tropical Medicine, UK.

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68

69 **Results**

70 The age of confirmed syphilis sero-reactive ranged from 17 to 53 years with a mean age of 31
71 years (SD=8.6). There were fewer females (29/471; 6.2%) than males (442/471; 93.8%). Of the
72 471 respondents, 28 (5.9%) donors gave a history of skin lesions and sores (Figure 1). Four
73 (14.3%) individuals out of the 28 donors with history of skin lesions and sores - all males and
74 RPR positive – recalled a diagnosis of syphilis. These four donors had previously received
75 penicillin treatment during their exposure to syphilis. Additionally, the four donors with a recall
76 of syphilis diagnosis reported appearance of lesions/bumps on skin and slow healing sores but
77 only one of them had these symptoms before the age of 15. This cannot even be clarified whether
78 this donor had yaws or syphilis at this young age although treated.

79

80 **Discussion**

81 The data presented here suggest that a clinical history of yaws is not frequent among syphilis
82 positive blood donors. However, syphilis symptoms were also not reported frequently. Children
83 aged below 15 years are the most vulnerable to yaws infection⁷. Only a small proportion of
84 confirmed sero-reactive donors had any recall of symptoms or treatment of yaws or syphilis.
85 Thus the relative contribution of yaws and syphilis to frequent positive tests in endemic areas
86 remains speculative. We have previously suggested combined specific and nonspecific syphilis
87 testing to identify potential infectious donors⁸. The present data suggest that clinical questioning
88 adds little further information to this screening algorithm. As a limitation, donors were
89 interviewed after knowing that they had a positive test for syphilis. This is a risk of recall bias

90 with reporting being influenced by the test results. There is furthermore a risk of
91 misclassification bias as many differential diagnoses exist for both syphilis and yaws.

92 However, despite these limitations the conclusion that clinical questioning adds little further
93 information when investigating syphilis sero-positive blood donors in areas where both
94 treponematoses exist seems solid.

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96

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102

103 ***Statement of Conflict of Interest***

104 None of the authors declare any conflict of interest regarding this manuscript.

105

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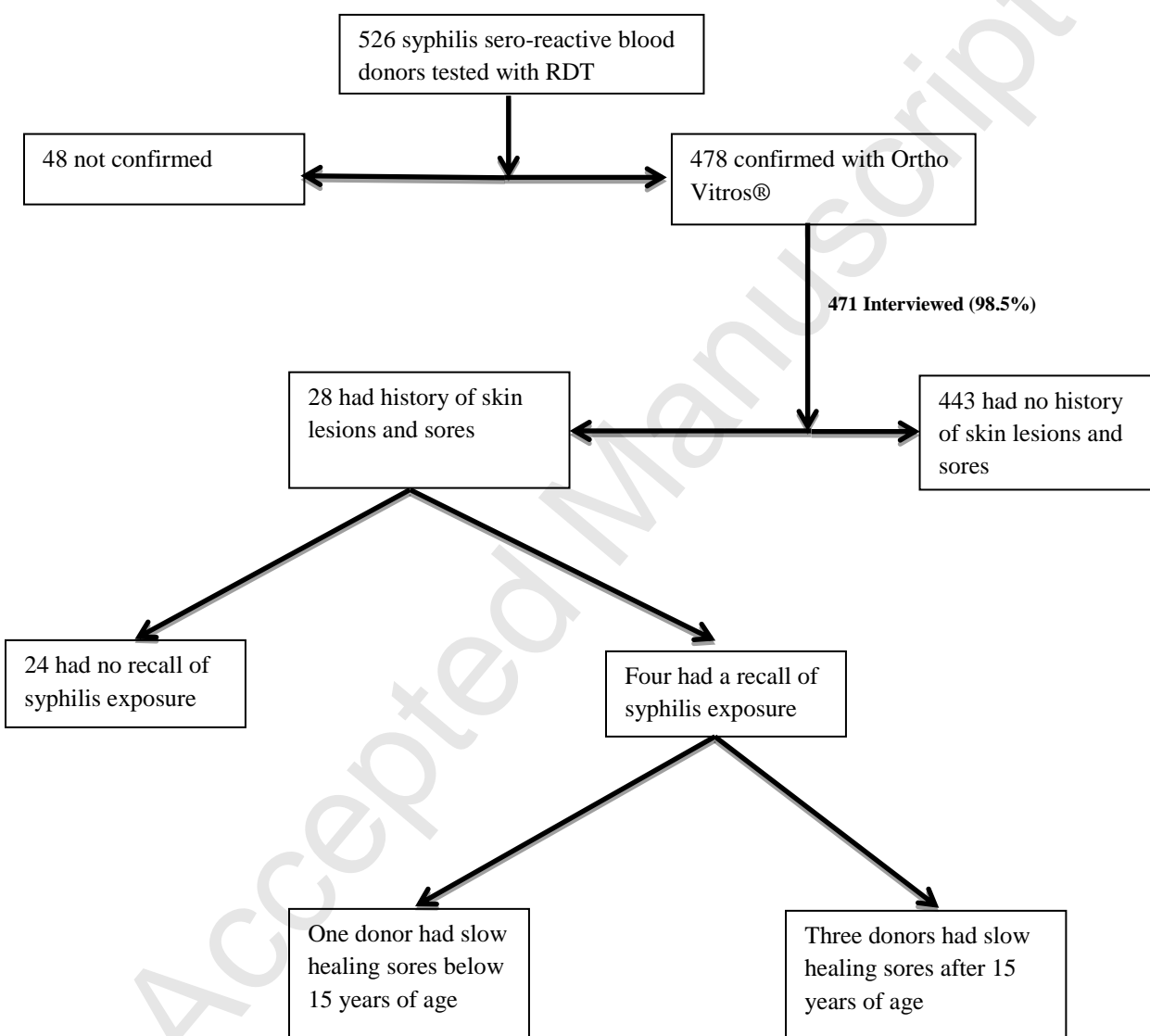
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155 Figure 1. A flowchart of syphilis sero-reactive blood donors interviewed for clinical
 156 manifestations of yaws

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162 **Highlights**

- 163 • A total of 478 syphilis sero-reactive blood donors from Komfo Anokye Teaching
164 Hospital, Kumasi, Ghana were confirmed with Ortho-Vitros® Syphilis TP test as gold
165 standard.
- 166 • We interviewed 471 consented (a response rate of 98.3%) syphilis sero-reactive blood
167 donors, to determine past or present clinical manifestations of yaws and syphilis.
- 168 • A total of 28 (5.9%) donors gave a history of skin lesions and sores.
- 169 • Four of the 28 donors (14.3%) who were all males and RPR positive, recalled a diagnosis
170 of syphilis with reported lesions/bumps on the skin and slow healing sores, but only one
171 of them had these before the age of 15.
- 172 • Our data suggest that a clinical history of yaws is not frequent among syphilis positive
173 blood donors. However, syphilis symptoms were also not reported frequently.

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