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Antenatal syphilis screening in sub-Saharan Africa: lessons learned from Tanzania

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Summary

OBJECTIVES To synthesise data from four recent studies in Tanzania examining maternal syphilis screening and its operational implementation in routine antenatal clinics (ANC), drawing lessons for strengthened antenatal services for the prevention of mother-to-child transmission (PMTCT) of HIV.

METHODS The impact of untreated maternal syphilis was examined in a retrospective cohort of 380 Tanzanian women. Effectiveness and cost-effectiveness of screening and single dose benzathine penicillin treatment were prospectively examined in 1688 pregnant women. Observation, interviews and facility audits were carried out in health facilities within nine districts to determine the operational reality of syphilis screening.

RESULTS Overall, 49% of women with untreated high titre syphilis experienced an adverse pregnancy outcome compared with 11% of uninfected women. Stillbirth and low birthweight rates among those treated for high- or low-titre syphilis were reduced to rates similar to those for uninfected women. The economic cost was $1.44 per woman screened and $10.56 per disability-adjusted life year saved. In the operational study, only 43% of 2256 ANC attenders observed were screened and only 61% of sero-reactive women and 37% of their partners were treated. Adequate training, continuity of supplies, supervision and quality control are critical elements for strengthened antenatal services, but are frequently overlooked.

CONCLUSIONS Maternal syphilis has a severe impact on pregnancy outcome. Same-day screening and treatment strategies are clinically effective and highly cost-effective, but there are significant challenges to implementing syphilis screening programmes in sub-Saharan Africa. Current PMTCT interventions present an opportunity to reinforce and improve syphilis screening. Increasing PMTCT coverage will involve similar operational challenges to those faced by syphilis screening programmes.

keywords antenatal clinics, syphilis screening, adverse pregnancy outcomes, prevention of mother to child transmission of HIV, cost-effectiveness, barriers, operational implementation, Tanzania, Africa

Introduction

With the global focus on the impact of the HIV/AIDS epidemic in many parts of the developing world, antenatal care policy and recent intervention studies have largely addressed the prevention of mother-to-child transmission (PMTCT) of HIV (Walker *et al.* 2002; Jackson *et al.* 2003; Stringer *et al.* 2003). However, the impact of other antenatal infections on pregnancy outcomes should not be forgotten. Syphilis seropositivity in sub-Saharan Africa is common, with up to 17% of pregnant African women attending antenatal clinics (ANC) having serological syphilis (Ratnam *et al.* 1982; Schultz *et al.* 1987; Guinness *et al.* 1988; Hira *et al.* 1990; Vuylsteke *et al.* 1993; Bam *et al.* 1994; Leroy *et al.* 1995; Mayaud *et al.* 1995, 1998; Qolohle *et al.* 1995; Mwakagile *et al.* 1996; Wilkinson *et al.* 1997). Maternal syphilis, left untreated, can have an impact on the developing foetus as devastating as that of maternal HIV infection. Maternal syphilis was found to be responsible for 26 and 42% of stillbirths in unscreened women in Malawi and Zambia, respectively, and 19% of spontaneous abortions after 20 weeks of gestation

(McDermott *et al.* 1993). Therefore, screening and treatment for syphilis has been recommended as a routine part of antenatal care (World Health Organisation 2001; Centers for Disease Control and Prevention 2002).

Management of maternal syphilis relies on serological screening in pregnancy and treatment with an injectable penicillin. The recommended treatment for primary, secondary and early latent syphilis infection is a single intramuscular dose of 2.4 million units (MU) benzathine penicillin, with three doses for late latent syphilis or syphilis of unknown duration (World Health Organisation 2001; Centers for Disease Control and Prevention 2002). However, there have been many problems with the practical implementation of these screening and treatment strategies in developing countries (Gloyd *et al.* 2001). First, often for practical reasons, the single dose regimen is implemented as the standard treatment for all stages of syphilis, although there are no data from randomized trials to support the effectiveness of either the single or multiple dose strategies. Secondly, there are limited data on the cost-effectiveness (CE) of various screening and treatment strategies in developing countries to guide policy-makers. Thirdly, there is little documentation of the operational challenges faced in the implementation of syphilis screening and treatment in order to implement it effectively. Thus, not surprisingly, there has been widespread failure to implement routine antenatal syphilis screening policies in many countries. A recent study found that syphilis testing was a routine part of antenatal care management in 17 of 22 (73%) countries in sub-Saharan Africa, but that in these 17 countries only 38% of pregnant women were actually screened (Gloyd *et al.* 2001).

To address these limitations, a recent paper called for multilevel assessments at national level of the opportunities for, and barriers to, effective implementation of antenatal syphilis screening (Hawkes *et al.* 2004). Responding to this call, we draw together data from several recent studies in Tanzania on syphilis in pregnancy in order to estimate the impact of untreated maternal syphilis, and the effectiveness and CE of on-site screening and single dose treatment in averting adverse pregnancy outcomes (Watson-Jones *et al.* 2002a, 2002b; Terris-Prestholt *et al.* 2003). In addition, operational data on routine implementation of syphilis screening at the primary healthcare (PHC) level are used to explore the barriers to wide-scale effective implementation (Oliff 2002). This paper highlights the challenges facing policy-makers in Africa trying to scale-up the implementation of this intervention to a national level; draws parallels with the situation facing HIV-PMTCT programmes, which involve similar activities such as screening, testing, treatment and partner management; and argues for mutual reinforcement and integration of syphilis and HIV-PMTCT programmes, thus exploiting the opportunity offered by increased funding and political commitment directed at HIV-PMTCT.

Materials and methods

Tanzania is amongst several countries that recommend single dose benzathine penicillin for the treatment of pregnant women with syphilis as national policy. In theory, women can thus be tested and treated on the same day if on-site syphilis screening at the ANC is operational (Watson-Jones *et al.* 2002a). National guidelines stipulate that syphilis screening should be performed as part of routine antenatal care in all Tanzanian health facilities, including dispensaries, with ANC attenders having a screening test at their first antenatal visit for each pregnancy (Watson-Jones *et al.* 2002a). In 1996, on-site syphilis screening was introduced at the main ANC in Mwanza city, and from 2000 in the whole of Mwanza Region, by the Ministry of Health with support from the African Medical and Research Foundation (AMREF), a healthcare non-governmental organization. All new attenders are screened for syphilis using the rapid plasma reagin (RPR) test. RPR-positive women are treated on the same day with a single dose of benzathine penicillin 2.4 MU and are given a partner notification slip and encouraged to send their partners to the clinic for free treatment.

To examine the effectiveness of this programme, several studies were carried out from 1997 to 2000. The detailed methods have been described elsewhere (Watson-Jones *et al.* 2002a, 2002b). First, to measure the impact of untreated maternal syphilis on birth outcomes, a retrospective cohort of 380 women admitted for delivery was recruited from three hospitals in Mwanza Region (Watson-Jones *et al.* 2002a). Women who had not been tested for syphilis during that pregnancy were screened by the RPR test (Syfacard®, Murex Diagnostics, UK). For every RPR-positive woman recruited, the next two RPR-negative women admitted were also enrolled. Birth outcomes [stillbirth, low birthweight (LBW), prematurity, intrauterine growth retardation and signs of congenital syphilis] were compared among (a) women with high-titre syphilis (HTS), defined as an RPR titre >1:8 and a positive specific treponemal test [*Treponema pallidum* agglutination assay (TPHA) Microsyph^{TM}-TP 1000, Porton, Cambridge, UK; or fluorescent treponemal antibody-absorption (FTA-ABS) assay, Trepo-Spot®-IF, Bio-Merieux, France]; (b) women with other serological stages of syphilis and (c) uninfected women (negative on both RPR and TPHA) (McDermott *et al.* 1993; Larsen *et al.* 1995). Data were collected on potential confounders for adverse birth outcome including

socio-demographic factors, maternal malaria and anaemia, maternal HIV and other reproductive tract infections. RPR-positive mothers and their infants were treated after birth where possible.

Secondly, to examine the effectiveness of antenatal screening and treatment, a prospective cohort of 1688 ANC attenders was recruited from the main ANC in Mwanza city (Watson-Jones *et al.* 2002b). For each RPR-positive woman enrolled consecutively, the next two RPR-negative women were also recruited and all were followed to delivery. Data on pregnancy outcome and potential confounders were collected as above.

Thirdly, the financial and economic costs of introducing syphilis screening into routine antenatal care services were measured and the CE of syphilis screening was calculated (Terris-Prestholt *et al.* 2003). CE ratios for LBW live births and stillbirths averted, and the cost per disability-adjusted life year (DALY) saved, both including and excluding stillbirths, were calculated. The CE of the intervention at different syphilis prevalence rates was modelled. The CE in Mwanza was compared with other CE studies of syphilis screening in sub-Saharan Africa as well as with other antenatal interventions, for which costs per DALY saved were calculated.

Fourthly, to examine the operational reality of implementing routine syphilis screening in public clinics in Tanzania, data were gathered in 2000/2001 from nine health facilities around the country (Oliff 2002). One facility was randomly sampled from each of three districts from three regions to represent the varied realities of health service delivery in Tanzania, with urban, roadside and rural sites being represented. In Mwanza Region (north-western Tanzania), one district hospital, one health centre, and one dispensary were selected; in Dodoma Region (Central), one district hospital, one health centre, and one dispensary were selected; and in Morogoro Region (Eastern), two health centres and one dispensary were selected. On average, 12–14 days were spent in each site observing clinical care, conducting interviews with staff and patients and carrying out systematic audits and client flow analyses. Data were collected on drug and diagnostic kit supplies and equipment for syphilis screening, health education sessions, ANC attendance rates for the previous four months, and the quality and frequency of staff training.

Ethics approval

Persons included in this study were self-presenting patients to routine clinics who accepted recording of their anonymized personal data. RPR-positive mothers and their infants were treated after birth where possible. The studies were approved by the ethical committees of the Medical Research Coordinating Committee of Tanzania and the London School of Hygiene and Tropical Medicine.

Results

Impact of untreated maternal syphilis

Untreated maternal syphilis was strongly associated with adverse birth outcome, especially in women with HTS (Watson-Jones *et al.* 2002a). Twenty-five per cent of the 73 women with HTS had a stillbirth compared with 1% of 233 seronegative women [risk ratio (RR) 18.1, $P < 0.001$]. HTS cases were also at higher risk of LBW and premature live births compared with uninfected women (adjusted RR 3.3 and 6.1, respectively). No association was found between other serological stages of syphilis and adverse birth outcomes. In this population, where 5.9% of women who had not been screened for syphilis in pregnancy had HTS, 51% of stillbirths, 24% of preterm livebirths and 17% of all adverse pregnancy outcomes in unscreened women were attributable to HTS. By identifying morbidity only at the time of delivery, our study may have underestimated the actual burden related to congenital syphilis, as many women with earlier stillbirths or miscarriages may not have attended.

Effectiveness of single-dose benzathine penicillin treatment

From September 1997 to December 1999, 19 878 women were screened at the main ANC in Mwanza and 1522 (7.7%) were RPR-positive. All RPR-positive women were treated with a single intramuscular dose of benzathine penicillin 2.4 MU on the day of screening. In total, 1688 women (556 RPR-positive and 1132 RPR-negative) were recruited to the cohort and 91% were followed to delivery.

Single-dose treatment was effective in preventing adverse outcomes attributable to maternal syphilis. There were no significant differences in birth outcomes between women treated for syphilis and seronegative women. Stillbirth and LBW live births were observed in 2.3 and 6.3% of treated HTS cases, and 2.5 and 9.2% of seronegative women respectively (Watson-Jones *et al.* 2002b). Controlling for potential confounders, women treated for either HTS [odds ratio (OR) 0.76, 95% confidence interval (CI) 0.4–1.4] or low-titre syphilis (OR 0.95, 95% CI 0.6–1.5) were at no increased risk of adverse pregnancy outcome compared with uninfected women. Overall, 37% (203/552) contacts of RPR-positive

Table 1 Syphilis serological status of male partners according to the serological status of index pregnant women in Mwanza, Tanzania

	Female index patients*			
Serological syphilis categories	TPHA pos / RPR pos >1:8 [HTS] ($n = 153$)	TPHA pos / RPR pos <1:8 [LTS] ($n = 275$)	TPHA neg/ RPR pos [BFP-RPR] ($n = 124$)	Total ($n = 552$)
Male partners				
Seen and tested	50 (33)	101 (37)†	52 (42)	203 (37)
Of whom				
TPHA pos/RPR pos >1:8 [HTS]	10 (20)	5 (5)	2 (4)	17 (8.5)
TPHA pos/RPR pos <1:8 [LTS]	6 (12)	18 (18)	1 (2)	25 (12)
TPHA pos/RPR neg [Old]	1 (2)	5 (5)	2 (4)	8 (4)
TPHA neg/RPR pos [BFP-RPR]	4 (8)	10 (10)	10 (19)	24 (12)
TPHA neg/RPR neg [No syphilis]	29 (58)	63 (62)	37 (71)	129 (63.5)

Values are given as *n* (%).
TPHA, *Treponema pallidum* haemagglutination assay; RPR, rapid plasma reagin test; HTS, high-titre syphilis; LTS, low-titre syphilis; Old, past or already treated/cured syphilis; BFP, biological false positive.
* For 27 women with 'Old syphilis' (TPHA+/RPR-) and 1056 women with 'No syphilis' (TPHA-/RPR-) partners were not sought and tested.
† Two partners of women with LTS attended but had incomplete syphilis results and have been omitted from total of those 'seen and tested'.

women attended, of whom 42 of 203 (21%) men with complete serology results were RPR-positive (any titre) and TPHA-positive (Table 1). Serological status of these men varied according to the serological status of the female index case: 32% (16/50) of male partners of HTS women had evidence of serological syphilis, *vs*. 23% (23/101) of male partners of low-titre syphilis (LTS) women, and 6% (3/52) of male partners of women with biological false positive RPR tests ($P = 0.003$) (Table 1).

Cost-effectiveness of syphilis screening and treatment

Syphilis screening in Mwanza was highly cost-effective. In 2001 US$, it was estimated to cost $1.44 per woman screened, $20 per woman treated and $187 per adverse birth outcome averted (Terris-Prestholt *et al.* 2003). The cost per DALY saved was $110 for cases of LBW averted, and $10.56 per DALY saved if stillbirths averted were also included. Costs per DALY saved were calculated from other published CE studies of syphilis screening from sub-Saharan Africa (Hira *et al.* 1990; Jenniskens *et al.* 1995; Fonck *et al.* 2001), by adjusting costs to constant 2001$ and performing a re-analysis of data using the same methodology as for this effectiveness study (Terris-Prestholt *et al.* 2003). These ranged from $10.56 to $18.73 per DALY saved, and studies had originally underestimated the CE of syphilis screening. Modelling showed that the CE of syphilis screening was highly dependent on syphilis prevalence, but was still cost-effective at a relatively low seroprevalence of 2% ($33 per DALY saved).

Operational performance of the syphilis screening programme

Screening. Observations in nine districts in 2000/2001 showed that many facilities were failing to implement syphilis screening effectively. During clinical observations of 342 ANC attenders across the nine district study sites, only 39% were either tested for syphilis, or had been booked for testing if screening was not underway in the clinic on the date the women attended. Examination of clinic registers confirmed the failure to capture a high proportion of women. Of 2256 ANC attenders eligible for syphilis screening over 4 months at these sites, only 970 (43%) were documented as receiving an RPR test, of whom 144 (15%) were RPR-positive. Of these cases, only 88 (61%) were treated and 53 (37%) had a sexual contact who attended the clinic for treatment (Figure 1).

Management. A lack of test kits and drugs at the time of the survey was observed. Each vertical programme, including antenatal care services and family planning, had its own system for ordering and restocking supplies. This led to duplication and confusion when requisitioning stocks. The number of facilities with the minimum supplies needed to test ANC attenders over 1 week and treat seroreactive women with benzathine penicillin was assessed, based on average weekly attendance of ANC attenders recorded in the clinic register over 4 months, and the average seroprevalence rate at the clinic. Only three sites were fully equipped to test and treat their ANC

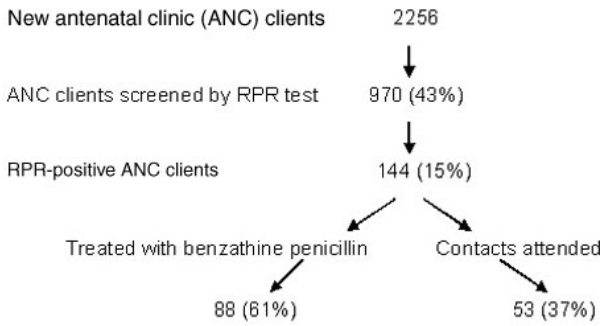

Figure 1 Proportion of antenatal clinic (ANC) clients tested and treated for syphilis over 4 months in nine district health facilities in Tanzania, 2000.

attenders for syphilis. Four sites had insufficient supplies to perform screening, and four sites did not have enough drugs (two sites lacked both kits and drugs). Furthermore, of the five sites with sufficient RPR testing kits, RPR testing was taking place in only two at the time of the survey. Condoms were available in sufficient quantities across all sites but one.

Performance of the health system. Other factors contributing to the failure to screen eligible women, including the skills and motivation of healthcare workers (HCW), are summarized in Table 2. Only 10% of 110 interviewed staff who were consulting with patients and likely to assess prenatal clients (including nurse midwives, trained nurses, nursing officers and nurse auxiliaries) had actually received training in performing the RPR test, and only two trained staff had ever received refresher training. Problems in maintaining screening services frequently arose because staff were absent from duty or had been transferred to another facility before a replacement had been trained. Because HCW believed that the pack of test cards within the RPR kits should be used completely once opened, like a vaccine vial, they instructed women to attend on specific days for testing, so negating the same-day testing and treatment protocol. ANC attenders were frequently asked to return on yet another day for treatment because nurses and maternal child health aides, who comprised 73% of the HCW trained in RPR testing, were not permitted to diagnose and treat medical conditions. There was a general lack of understanding among HCW at all sites about the implications of untreated maternal syphilis and screening was not perceived as a high priority. Interviews with senior ANC staff revealed that performing the RPR test itself was an unpopular, time-consuming task, requiring one HCW to manually rotate each RPR testing card for 8 min. At the technical level, procedures for quality control of RPR screening were not in place at any of the district sites. RPR antigen vials were stored at room

Table 2 Operational barriers to implementing syphilis screening programme at the primary healthcare level in nine districts of Tanzania

Failure to screen and treat eligible antenatal clinic attenders	
Lack of RPR testing kits, drugs and consumables	Different drug and consumables ordering and supply systems in Tanzania for ANC, FP, STI programmes: (i) Burden on HCW, (ii) Complex and time-consuming, (iii) Inadequate STI drug supply; drugs 'borrowed' from ANC stocks
HCW factors	Belief among HCW that syphilis prevention in pregnancy is low priority Often one person trained in RPR test at each site: (i) Transferred before a replacement trained, (ii) No cover for leave/illness, (iii) No refresher training, (iv) Lack of understanding of rationale behind screening, (v) Screening is unpopular and time-consuming Belief that kits must be used in entirety therefore HCW postpone screening Lack of HCW trained to give injections preventing same-day treatment Lack of antibiotic prescribing authority for nurses
Performance and quality of RPR screening	
Performance, quality control and storage	Rate of biological false positive results probably too high No quality control procedures in place Storage of RPR test kits inadequate
HCW/health system factors	No refresher training of HCW Lack of adequate supervision of HCW

RPR, rapid plasma regain; ANC, antenatal clinic; FP, family planning; STI, sexually transmitted infections; HCW, healthcare workers.

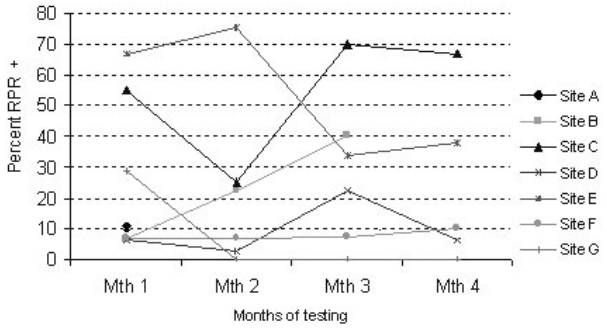

Figure 2 Monthly rapid plasma reagin positivity rates among antenatal clinic attenders over 4 months, in seven district facilities implementing syphilis screening programme in Tanzania, 2000.

temperature in all the districts as the Expanded Programme of Immunization refrigerators were considered to be reserved for vaccines.

The district health management teams routinely made quarterly supervision visits to the health facilities. These were usually administrative visits, rather than providing technical supervision. There was no supervision of quality of care and examination of clinic registers showed wide fluctuations in monthly RPR prevalence rates that were neither detected nor acted upon during these supervision visits, despite the fact that they suggested variability in test performance (Figure 2).

Discussion

Single dose treatment of syphilis is effective and cost-effective

Maternal syphilis, left untreated, continues to be an important risk factor for adverse pregnancy outcome in Tanzania (Watson-Jones *et al.* 2002b; Terris-Prestholt *et al.* 2003). This risk is especially high in mothers with high RPR test titres, observed in earlier stages of infection (Watson-Jones *et al.* 2002a), and is consistent with an earlier African study (Schultz *et al.* 1987). There remain no data from randomized trials comparing single with triple dose benzathine penicillin therapy, but our data suggest that single dose treatment is effective in preventing stillbirth and LBW in women with syphilis, including those with HTS, the stage of untreated syphilis most strongly associated with poor birth outcome (Watson-Jones *et al.* 2002b).

Our cost analysis of syphilis screening and treatment in Tanzania also shows that this is a highly cost-effective intervention (Terris-Prestholt *et al.* 2003). Earlier studies estimated that the cost of antenatal syphilis screening compared well with other childhood interventions (Schultz *et al.* 1992). In the context of the HIV epidemic in Africa, the cost of syphilis screening and treatment ($10.56 per DALY saved) compares favourably to that of nevirapine treatment for HIV-PMTCT in Uganda ($11.19) (Marseille *et al.* 1999).

Routine implementation faces operational obstacles

The reality, however, is that antenatal syphilis screening is failing across sub-Saharan Africa. Based on the limited coverage from 22 African countries (Gloyd *et al.* 2001), it has been estimated that with these coverage levels and a mean 8.3% prevalence of active syphilis, approximately 630 000 women are screened and treated while another 1 640 000 seropositive pregnant women remain untreated, of whom 1 030 000 (63%) will have attended antenatal services. Assuming RPR-positive women would have similar rates of HTS as in Mwanza (27%) and that they would experience a similar rate of adverse outcomes as observed in untreated women in Mwanza (49%) (Watson-Jones *et al.* 2002a), a total of 136 269 adverse birth outcomes could potentially be averted by screening and treatment.

In principle, a single visit for on-site testing and same-day treatment should improve the uptake of syphilis screening (Watson-Jones *et al.* 2002a). This is important in the context of sub-Saharan Africa where women frequently fail to re-attend for treatment (Jenniskens *et al.* 1995; Fonck *et al.* 2001). Despite the fact that Tanzania has decided to implement a decentralised screening service, however, a disappointingly low proportion of ANC attenders are successfully screened and treated at PHC level.

Screening and single-dose treatment are clinically effective and cost-effective, and the procedures are simple, implying that antenatal syphilis screening should be feasible and affordable. What remain to be addressed, however, are the operational barriers at the ANC level, as well as the political will and financial constraints within the health system.

Obstacles to successful implementation include the organization of services, costs of treatment, transport costs to health facilities performing testing and low priority at government level (Gloyd *et al.* 2001), as well as staff training, monitoring, quality control and logistics. Improvements can be effective, as shown by an evaluation of the antenatal syphilis screening programme in Nairobi, which currently has a 3.4% RPR seroprevalence. Overall, 91% of RPR-positive women received prompt treatment (Fonck *et al.* 2001). The programme started with an intensive monitoring and evaluation phase in 1993 but, over time, observed a decline in the quality of RPR testing (Fonck *et al.* 2001). The authors concluded that maintaining a high level of quality control and supervision was

Table 3 Advantages and limitations of *Treponema*-specific rapid diagnostic tests for on-site antenatal syphilis screening

Advantages
Simplicity and speed (some tests can use whole blood rather then serum)
Reduces the time-consuming procedure of serum separation
Avoids 8-min shaking procedure required for RPR test
Shorter waiting time for patient to receive results
In most cases these tests are easier to read than agglutination tests
May reduce need for staff training and quality control that is essential to maintain screening performance using subjective RPR test
Less subjective therefore improves the performance of on-site syphilis testing
Less expensive (Some tests can use a finger-prick specimen of capillary blood)
Lancets are cheaper than needle and syringes or vacutainer systems
No RPR test cards or test-tubes or racks required
Reagents can in most cases be stored at room temperature
Treatment costs for women with biological false positive RPR reactions would be avoided
Limitations
Finger prick blood can be messy to handle
Patient's preference for venous blood collection which appears more 'serious' in some settings
Cannot distinguish between past and present infections
Lifetime positivity means difficulty in interpretation in subsequent tests – may require 'confirmatory' RPR test
Cost of tests still high

difficult, and may be impossible in some remote settings, and that in Nairobi mass treatment with penicillin in pregnancy may be equally cost-effective. However, the acceptability and effectiveness of this strategy are unproven.

Further research is needed on several specific components of syphilis screening programmes. The simple and cheap RPR test, recommended as a suitable screening test for syphilis (World Health Organisation 2001; Centers for Disease Control and Prevention 2002), is time-consuming, subjective to interpret and therefore requires some experience to recognize a positive test. Although the RPR antigen is relatively stable at room temperature (van Dyck *et al.* 2001), storage between 2 and 8 °C is recommended, which is difficult at the PHC level. It is unclear how much this affects test performance as there are few sites implementing regular quality control exercises. Our observations in Tanzania also highlight the difficulties in ensuring that HCW actually perform this test and show that there are basic misunderstandings about the testing procedure. In Nairobi, there was also wide variation in performance at different clinics within the city (Jenniskens *et al.* 1995). Wide variations are likely in other countries where refresher training and quality assurance of programme activities are infrequent.

There has long been an urgent need for simple rapid screening tests for syphilis and other STI. Several dipstick-type *Treponema*-specific serological tests for syphilis are now on the market (Mabey and Peeling 2002). These new tests, whose advantages and limitations are shown in Table 3, could greatly simplify ANC syphilis screening, because of their ease of use even under the most rudimentary conditions. Like other *Treponema*-specific tests, however, they do not distinguish between previously treated and untreated infections and, in areas of high syphilis prevalence, these tests may best be used in conjunction with RPR results.

Treatment of sexual partners is a recommended component of syphilis programmes in order to prevent congenital syphilis because of maternal re-infection (World Health Organization 2001; Centers for Disease Control and Prevention 2002). The CE of this strategy has never been rigorously evaluated in sub-Saharan Africa (Mathews *et al.* 2001). First, there are few data on its actual efficacy. One study in Nairobi found that RPR-positive women whose partners attended for treatment had a better pregnancy outcome than those whose partners did not attend (Gichangi *et al.* 2000). However, this analysis was not adjusted for other variables that might have influenced birth outcome. Secondly, the effectiveness of the intervention would depend on its coverage. In Tanzania, uptake of treatment by partners has proved to be low (Watson-Jones *et al.* 2002b), as in other countries where it varies between 15 and 75% (Jenniskens *et al.* 1995; Gichangi *et al.* 2000; Fonck *et al.* 2001). Barriers to successful partner notification in Africa include inadequate counselling, short-term or casual relationships and fear of informing partners (St Louis 1996; Fonck *et al.* 2001). Thirdly, doubts have

been raised as to whether partner notification has any practical impact on syphilis transmission because those most at risk of infection may not be traceable or may not choose to attend for treatment (Andrus *et al.* 1990; St Louis 1996). Certainly, both in Mwanza and South Africa (Donders *et al.* 1997), over 60% of contacts presenting to the clinic were syphilis seronegative. In our study, overall 42 of 203 (21%) attending male contacts with complete serology results were RPR and TPHA positive. The rate of seropositivity was significantly higher among partners of women with HTS (32%), but a strategy targeting partners of women with a confirmed RPR test (either HTS or LTS), or indeed only women with HTS, would fail to identify a high proportion of truly infected men: 7% (3/42) in the former group, 62% (26/42) in the latter. In summary, there are insufficient data from developing countries on the quality of partner notification, the consequences for the infected index case and their contacts, the CE and overall impact on syphilis transmission of any contact tracing strategy, but there is some evidence that it identifies a significant number of men who otherwise would be left untreated.

Despite these uncertainties, it is important that policy makers and HCW recognize that syphilis screening is an essential component of antenatal care. Moreover, we know that syphilis is capable of re-emerging in populations extremely rapidly when prevention efforts decline or collapse (Nanda *et al.* 1990; Imperato 1991; Cossa *et al.* 1994; Borisenko *et al.* 1999). There is an array of cheap and simple screening tests, an effective treatment, and the cost per DALY saved is at least comparable with that of HIV-PMTCT. Furthermore, there is evidence that antenatal syphilis screening may help to reduce the heterosexual transmission of syphilis as the prevalence of syphilis is declining in sites such as Nairobi where screening and partner notification have been implemented for some years (Temmerman *et al.* 1999).

Integration and sharing lessons learned

Syphilis screening as a routine antenatal intervention must not be neglected in the context of initiatives to prevent maternal transmission of HIV. Syphilis might not carry the same stigma associated with HIV, given the relatively high rate of women accepting the tests, and of their male partners coming forward, and because syphilis is a curable disease. Indeed, HIV surveillance and interventions have often been piggy-backed onto antenatal syphilis screening services. Conversely, efforts to provide wide-scale HIV-PMTCT programmes would provide an excellent opportunity to strengthen antenatal syphilis screening. Both interventions are aimed at the same target population, are sited in the same facilities, face similar logistical challenges, involve the same HCW and require a blood sample to be taken after pre-test discussion. At present, however, HIV prevention and treatment services are often organized vertically, and this is likely to lead over time to increased costs and fragmentation as observed in other vertical programmes. The need to develop models of integration must be addressed now, while PMTCT initiatives are still in their developmental phase.

Studies in South Africa, Nairobi and Mwanza have demonstrated that effective syphilis screening programmes can be implemented through the PHC system if these programmes are given sufficient support through training, adequate supervision and availability of resources, and that these programmes are capable of significantly reducing adverse pregnancy outcomes attributable to syphilis (Wilkinson & Sach 1998; Temmerman *et al.* 2000; Watson-Jones *et al.* 2002b). Data on the implementation of PMTCT programmes suggest that there are a number of problems related to achieving coverage and retention of patients, and that costs are much higher than in pilot or trial conditions (Stringer *et al.* 2003). Experience from syphilis screening also highlights the potential problems faced by new PMTCT programmes as they try to increase coverage. Adequate training, continuity of supplies of testing kits, consumables and drugs, supervision and quality control are all essential if the quality of the intervention is to be sustained.

There is a need for genuine recognition by donors and policy makers that syphilis control and PMTCT of HIV are complementary. PMTCT programmes have a much larger funding base and their system requirements are greater but they will likely remain poorly implemented in areas where there are currently no sustainable systems for syphilis screening and management. PMTCT of HIV, maternal syphilis screening and other ANC interventions would benefit greatly from closer collaboration as part of an integrated reproductive health programme. As governments grapple with decentralization of health services, integration would help to ensure that evidence-based ANC interventions such as syphilis screening, malarial prophylaxis and vitamin supplementation do not drop off the agenda in the face of pressure to implement HIV-PMTCT through vertical programmes.

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