

ORIGINAL ARTICLE

Universal Prevention is Associated with Lower Prevalence of Fetal Alcohol Spectrum Disorders in Northern Cape, South Africa: A Multicentre Before–After Study

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(Received 25 June 2011; in revised form 28 September 2011; accepted 29 September 2011)

Abstract — **Aims:** Prevalence of fetal alcohol spectrum disorders (FASDs) is remarkably high in several provinces of South Africa; yet population-level knowledge of the harms of maternal drinking remains low. In two heavily affected areas, we assessed effectiveness of interventions to heighten awareness of these harms and to alter social norms about drinking in pregnancy. **Methods:** FASD prevalence, maternal knowledge and drinking behaviours were investigated in two Northern Cape Province towns, before and after interventions which included highlighting FASD using local media and health promotion talks at health facilities. Independently, two dysmorphologists and a neuropsychometrist examined children at 9 and 18 months. **Results:** Pre-intervention maternal knowledge of alcohol harms was low and FASD prevalence 8.9% (72/809). Interventions reached high coverage and knowledge levels increased substantially. FASD prevalence was 5.7% post-intervention (43/751; $P=0.02$); 0.73 lower odds, controlling for maternal age and ethnicity (95% confidence interval=0.58–0.90). No change was detected in more severe FASD forms, but in the whole population, median dysmorphism scores reduced from 4 [inter-quartile range (IQR)=2–7] to 3 (IQR=1–6; $P=0.002$). **Conclusion:** This, the first prevention study using FASD outcomes, suggests that universal prevention might reduce FASD by ~30% and have population-level effects. This supports intensifying universal interventions where knowledge of harms of maternal drinking is low. These efforts need to be accompanied by alcohol-dependence treatment to lower more severe FASD forms.

INTRODUCTION

Fetal alcohol spectrum disorder (FASD) is among the commonest causes of learning disability worldwide, and is eminently preventable (American Academy of Pediatrics, 2000). Globally, some of the highest rates occur in South Africa, and while no systematic surveillance system is in place, several studies suggest levels are increasing (May *et al.*, 2000; Urban *et al.*, 2008). In the late 1990s, a study in Wellington in the Western Cape Province reported a prevalence of FASD of 40.5–46.6 per 1000 children 5–9 years (May *et al.*, 2000). Two subsequent surveys in the same area, using similar methods reported even higher levels of between 65.2–74.2 per 1000 children in 2000 (Viljoen *et al.*, 2005) and then 68.0–89.2 per 1000 children in 2002 (May *et al.*, 2007). Between 2001 and 2004, among the highest ever reported FASD rates were found in school-entry children in two towns in the Northern Cape Province, De Aar (119.4/1000) and Upington (74.7/1000) (Urban *et al.*, 2008). Clearly, South Africa has a massive and even increasing FASD burden.

The most common drinking pattern in pregnant women that results in FASD is heavy-episodic (binge) drinking. This drinking pattern, common among women in many parts of South Africa (Peltzer and Ramlagan, 2009; Ojo *et al.*, 2010), is amenable to intervention, as it is not necessarily associated with alcohol dependence (WHO, 2001a). Universal approaches to FASD prevention aim to increase population-level understanding of the harms of alcohol use in pregnancy and thereby shift drinking norms. In indicated prevention, high-risk individuals receive interventions, such as women with alcohol dependence or those who already have a child

with FASD (Astley *et al.*, 2000). Most FASD prevention studies to date have tested a third prevention modality, selective interventions. This often involves screening pregnant women for alcohol use and then providing, for example, brief interventions for those at high risk (Stratton K *et al.*, 1996; Hankin, 2002, Centers for Diseases Control and Prevention 2009; Floyd *et al.*, 2009). A systematic review identified only four FASD prevention trials, which together suggested that brief psychological and educational interventions may reduce alcohol use among pregnant women (Stade *et al.*, 2009). No studies had FASD diagnosis as a study endpoint.

This study assessed whether FASD prevalence would be reduced by universal interventions to raise community and health worker awareness of the harms of maternal drinking and to shift-related social norms. Changes in FASD prevalence, and in maternal knowledge and drinking behaviour, were assessed in two small South African towns before and after interventions provided mainly by community workers and through the local media.

MATERIALS AND METHODS

The study was conducted in De Aar and Upington, towns in the arid Northern Cape Province, populated predominately by people of mixed ancestry. Both towns have high indices of socio-economic deprivation (Bureau of Census, 2001). De Aar is a railway and sheep farming centre with about 28,000 inhabitants, whereas Upington is a viticulture area of 58,000 people on the banks of the Orange River. The study took place from 2003 to 2006 in De Aar and from 2005 to 2010

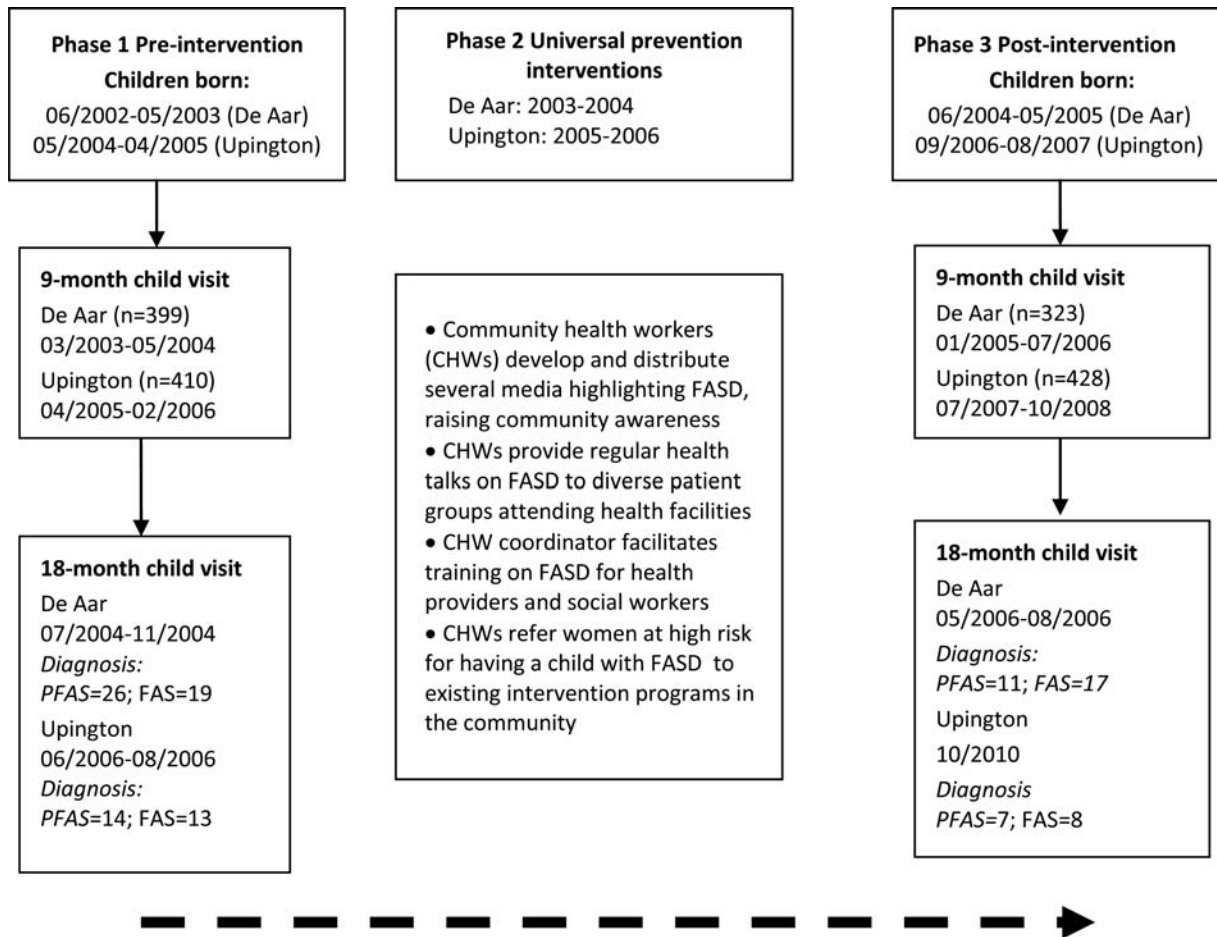


Fig. 1. Flowchart of the three study phases of the FASDs prevention study.

in Upington (Fig. 1). There were three study phases: firstly, a baseline assessment of fetal alcohol syndrome (FAS) and partial FAS (PFAS) prevalence; secondly, prevention interventions; and, finally, 1 year thereafter, assessment of FAS/PFAS prevalence (Fig. 1).

Before and after the prevention intervention, cohorts of infants, born in a 1-year period, were identified through birth records collected from public-sector hospitals. In both phase one and three in De Aar, we attempted to trace all children born in each 1-year period. As Upington has a larger population, in both phase one and three, a random sample of about half the children was selected from a list of all births in each 1-year period. A random number table was used in this selection. In both sites, community-health workers (CHWs) used contact information from birth records to trace the infants' mothers or guardians (if the mother was unavailable or deceased). Women who had moved from the area between childbirth and the time of the interview were excluded.

Phase one and three: assessing study outcomes before and after intervention

Identical procedures were used in phases one and three. Birth weight was obtained from hospital records, and maternal age, ethnicity and infant anthropometry were collected from participants at the 9-month visit. Infant length was

measured using rubber Measure Mats. A structured questionnaire, previously developed and tested in the local population (Viljoen DL *et al.*, 2003), was administered by a trained counsellor or neuropsychometrist to mothers. Guardians completed abbreviated proxy interviews. Interviews measured demographics, socio-economic exposures and alcohol use in FAS/PFAS cases and an equal number of controls, matched for ethnicity and infant age. Beck's Depression Inventory was used to screen for maternal depression (Beck *et al.*, 1961; Ward *et al.*, 2003). We assessed alcohol use in the period around the time of the interview and during pregnancy using a timeline follow-back method (Sobell *et al.*, 2001). Maternal knowledge and attitudes to alcohol use, and the amount of exposure to the intervention were also assessed.

Infants were examined for dysmorphic features and neurological signs at 9 months and those with evidence of FAS/PFAS were re-examined at 18 months, alongside control infants. To standardize assessment of dysmorphic features, a checklist (May *et al.*, 2000) was used to yield a dysmorphology score, with a maximum score of 35. All infants were evaluated independently by two trained clinicians, skilled in diagnosing FAS/PFAS. Infants with features suggesting FAS/PFAS and control infants had a developmental assessment using the Griffiths Mental Development Scale (Griffiths R, 1970), validated in some South African

populations (Adnams *et al.*, 2001). Development was evaluated over the following modalities: locomotor; personal-social; hearing and speech; eye-hand coordination; skills in manipulation and speed of performance and executive functioning. Subscale quotients for each skill area were derived independently, and a general developmental quotient obtained by combining the subscale scores. If developmental indices could not be determined due to very low test scores, an index score of 50 was assigned. For FAS/PFAS diagnostic purposes, infants were classified as having neurocognitive delay if any of the subscales were ≤ 68 (2 standard deviations below the expected mean of 100), or the general developmental total score was ≤ 84 (1 standard deviation below expected mean) (Griffiths R, 1970).

A FAS diagnosis was made when infants had the characteristic facial phenotype (including small palpebral fissures, midface hypoplasia, smooth philtrum and thin vermilion border); growth deficiency (≤ 10 th percentile for height, weight or head circumference) and documentation of central nervous system abnormalities (Hoyme *et al.*, 2005). Clinical diagnoses of FAS, but not PFAS, are considered distinctive even in the absence of a history of maternal alcohol consumption in pregnancy (National Center on Birth Defects and Developmental Disabilities *et al.*, 2004; Hoyme *et al.*, 2005). In addition to confirmation of maternal drinking, a PFAS diagnosis also required at least two of the three characteristic FAS facial features and one of growth retardation, neurological abnormality or abnormal neurocognitive assessment (Hoyme *et al.*, 2005). Only FAS/PFAS cases were assessed, in particular cases of alcohol-related neurodevelopmental disorder (ARND) were not ascertained, as the more subtle neurological features of this disorder are harder to detect in infancy. Final diagnoses were made in a case conference, reviewing all available data. For analysis purposes, FAS and PFAS cases were combined, forming the FAS/PFAS group.

Phase two: universal FASD prevention interventions

At baseline, prior to the prevention activities, coverage of interventions to educate women about the harms of drinking during pregnancy was relatively low. Only 39.5% (30/76) of cases and controls recalled having received information about FASD on the radio or television, while about two-thirds reported receiving this information from a nurse. In phase two, FASD prevention activities were provided using multiple platforms, over 1 year. Three trained CHWs led activities in each site. They received a monthly stipend and were supervised by full-time study coordinators (professional nurses). With input from local community representatives, a pamphlet and poster were designed and distributed to antenatal clinics, shops, taverns, government departments and prisons. Regular articles focusing on FASD prevention, and emphasizing the responsibility of both parents and the community for its prevention, were published in local community newspapers and reinforced by regular advertisements on the local community radio. Local drama productions on FASD themes were performed.

Community workers presented 'health talks' at clinics for infants and young children, family planning and antenatal care and at church and community meetings. These addressed a range of topics such as nutrition, breastfeeding

and family spacing, but were always underscored by messaging on FASD prevention. Training workshops on FASD were held for provincial and district-level staff from the Departments of Health and Social Services. FASD prevention messages were mainstreamed within the Department of Health's activities and in their interactions with the public, with FASD topics given prominence in all National Health Promotion events, such as Women's Day, Pregnancy Education Week, International FASD Day and Breast Cancer Awareness Month.

Study measures and analysis

Single data entry was done in a Microsoft Access 2003 (Microsoft, Redmond, WA, USA) database, and Intercooled Stata version 10.1 (Stata-Corp, LP, College Station, TX, USA) used for analysis. Prevalence of study outcomes was compared before and after the intervention. The primary outcome was FAS/PFAS prevalence. Secondary outcomes were: maternal knowledge about harms of alcohol use during pregnancy; self-report of maternal alcohol consumption; birth weight; infant anthropometry; neurodevelopment subscales and dysmorphology scores. As there were few white or Asian participants, these groups were combined with Black-Africans and outcomes in this group compared with people of mixed ancestry (79.1% of the population).

The χ^2 test detected differences between categorical variables, and a χ^2 test for trend assessed whether there was an increasing trend in proportions over exposure categories. For continuous variables, an unpaired Student's *t*-test or Mann-Whitney *U*-test compared data with a normal and non-normal distribution respectively. Infant anthropometric data were analysed using *z*-scores computed with the WHO Child Growth Standards program in Stata (WHO Anthro. Child Growth Standards). Multivariate logistic regression models investigated whether study phase was associated with FAS/PFAS diagnosis, controlling for maternal age, ethnicity and study site. As other socio-demographic data were only collected in a population subset (PFAS/FAS cases and controls) these variables were not included in multivariate models.

Ethical considerations

Study activities were approved by the University of Witwatersrand Human Research Ethics Committee. Informed consent was obtained from the mothers or guardians willing to participate. Throughout the study, women showing signs of alcohol dependence or children diagnosed with FASD were linked with a local alcohol treatment centre and the Department of Social Services. Assistance was offered in accessing government welfare grants, where applicable. The study team also provided some support for women with alcohol dependence or children with FASD through, for example, creating a toy library and play group, aimed at promoting early childhood development and maternal bonding. Women diagnosed with depression, an important FASD risk factor (Meschke *et al.*, 2003; Parker *et al.*, 2010), were referred for treatment and to local support groups. Children with FASD were linked with speech and hearing therapists, and occupational therapists. Malnourished children were referred to a dietician and enrolled into a local protein-energy malnutrition program.

RESULTS

In the pre-intervention phase, 809 children were enrolled (399 in De Aar and 410 in Upington), and 751 participated post-intervention (323 and 428 in the corresponding towns). Of the 500 births in the past year in De Aar phase one, 399 infants were located and enrolled (79.8%). Participation rates were very similar in Upington phase three—428 enrolled of the 538 birth records selected. Participation information is not available for De Aar phase three and Upington phase one. Field workers reported that very few women located declined to participate, non-participation was predominately due to women having moved or addresses in the birth records being incorrect or incomplete. At first examination, children were a median 10.5 months [inter-quartile range (IQR) = 9.7–11.4], and an average 2.5 weeks older in the post-intervention group (Table 1). Slightly more than half the infants were female

(50.5%), while 57.4% of FAS/PFAS infants were female. Maternal age at the time of the 9-month visit was similar in each phase, an overall mean 27.2 years (sd = 6.6), with 13.5% aged above 35 years (195/1444). The majority of women were of mixed ancestry (79.1%, 1186/1500), with the remainder mostly black (19.0%, 285/1500). Among cases and controls, three-quarters of pregnancies were unplanned (124/167), similar in phases one and three. No change was detected in unemployment levels between the phases.

The 84.0% of cases and controls who ever drank alcohol (158/188), recalled having their first drink at a mean 18.6 years (sd = 3.8). Alcohol debut was similar between phases, and in FAS/PFAS and non-FAS/PFAS cases, but was earlier in De Aar (17.7 years) than Upington (20.3 years; $P < 0.001$). Prior to the study intervention, only about half the cases and controls were aware that drinking in pregnancy could harm the fetus.

Table 1. Socio-demographic characteristics of women and infants before and after an intervention to reduce FASDs in Northern Cape, South Africa

Variable	Before intervention (A)	After intervention (B)	P (A vs. B)	FAS/PFAS cases before intervention (C)	FAS/PFAS cases after intervention (D)	P (C vs. D)
Whole study population in both sites						
Infant age at examination ^a median months (IQR), n	10.2 (9.5–11.0), 801	10.8 (9.9–12.0), 720	<0.001	10.4 (9.3–11.1), 72	11.2 (9.7–13.0), 42	0.01
Infant gender n female/ N (%)	413/793 (52.1)	357/730 (48.9)	0.22	40/72 (56)	26/43 (61)	0.61
Maternal age ^b mean years (sd), n	27.2 (6.4), 769	27.4 (6.8), 677	0.62	32.3 (5.8), 68	33.0 (6.2), 35	0.54
Ethnicity n/N (%)						
Mixed ancestry	608/776 (78.4)	578/724 (79.8)	0.48	66/72 (92)	41/43 (95)	0.45
Black, Asian and whites	168/776 (21.7)	146/724 (20.2)		6/72 (8)	2/43 (5)	
Cases and controls in both sites						
Marital status n/N (%) ^c						
Single	81/127 (63.8)	47/65 (72.3)	0.49	40/69 (58)	21/34 (62)	0.81
Married/engaged	26/127 (20.5)	10/65 (15.4)		13/69 (19)	7/34 (21)	
Living together	20/127 (15.8)	8/65 (12.3)		16/69 (23)	6/34 (18)	
Parity n/N (%) ^c						
1	28/126 (22.2)	14/64 (21.9)	0.96	7/69 (10)	5/33 (15)	0.57
2	39/126 (31.0)	19/64 (29.7)		18/69 (26)	8/33 (24)	
3	24/126 (19.1)	11/64 (17.2)		18/69 (26)	5/33 (15)	
≥4	35/126 (27.8)	20/64 (31.3)		26/69 (38)	15/33 (45)	
Highest education n/N (%) ^c						
None or primary incomplete	32/121 (26.5)	18/63 (28.6)	0.87	24/62 (39)	14/32 (44)	0.66
Primary complete	16/121 (13.2)	6/63 (9.5)		11/62 (18)	3/32 (9)	
Secondary incomplete	56/121 (46.3)	29/63 (46.0)		25/62 (40)	13/32 (41)	
Secondary complete	16/121 (13.2)	10/63 (15.9)		2/62 (3)	2/32 (6)	
Tertiary	1/121 (0.8)	0/63 (0.0)		0/62 (0)	0/32 (0)	
Employment n/N (%) ^c						
Unemployed	106/125 (84.8)	47/61 (77.1)	0.42	57/67 (85)	25/32 (78)	0.61
Temporary worker	10/125 (8.0)	8/61 (13.1)		6/67 (9)	5/32 (16)	
Full time employed	9/125 (7.2)	6/61 (9.8)		4/67 (6)	2/32 (6)	
Maternal depression n/N (%) ^c						
None	33/117 (28.2)	11/55 (20.0)	0.5	18/62 (29)	3/29 (10)	0.04
Mild depression	22/117 (18.8)	8/55 (14.6)		9/62 (15)	2/29 (7)	
Clinical depression	22/117 (18.8)	11/55 (20.0)		8/62 (13)	7/29 (24)	
Moderate depression	25/117 (21.4)	18/55 (32.7)		13/62 (21)	13/29 (45)	
Severe depression	15/117 (12.8)	7/55 (12.7)		14/62 (23)	4/29 (14)	
Tobacco use during pregnancy n/N (%) ^c	69/124 (55.7)	34/63 (54.0)	0.83	49/64 (77)	23/33 (70)	0.46

Data from whole study population and χ^2 test used unless indicated.

FAS, fetal alcohol syndrome; PFAS, partial fetal alcohol syndrome; IQR, inter-quartile range; sd, standard deviation.

^aMann–Whitney U -test.

^bStudent's t -test.

^cData on cases and controls, not the whole population.

Outcomes before and after study intervention

At baseline, FAS/PFAS prevalence was 8.9% (72/809) and 5.7% post-intervention (43/751, $P=0.02$; Table 2). The largest change between the phases was a halving of PFAS prevalence (4.9%, 40/809 to 2.4%, 18/751; $P=0.008$). In multivariate analysis, controlling for maternal age, ethnicity and study site, odds of FAS/PFAS was 0.73 lower in phase three than one [95% confidence interval (CI) adjusted odd ratio (AOR) = 0.58–0.91; Table 3]. Dysmorphology scores of the whole study population were lower in phase three (median score of 4 in phase one, IQR = 2–7; versus 3 in phase three, IQR = 1–6; $P=0.002$). No difference in infant head circumference was noted between all infants in phase one and three, while comparisons of infant weight (higher in phase three) and length (higher in phase one) yielded divergent findings.

Few differences between the phases were detected in the outcomes measured only in the cases and controls. FAS/PFAS mothers pre-intervention reported drinking a median of 14.9 units a week during pregnancy (IQR = 4.7–31.4), compared with 5.8 median units/week in FAS/PFAS mothers post-intervention (IQR = 3.0–13.2; $P=0.04$). Changes in volume drunk were, however, only detected in the PFAS group (17.6 median units/week in phase one versus 7.2

units/week in phase three; $P=0.05$) and not in volumes among women with a FAS child (7.8 median units/week in phase 1 and 4.4 median units/week in phase 3; $P=0.44$). In the first phase, about half of women who drank in pregnancy reported changing the amount they drank during pregnancy (31/63), and 60% reported this in phase three (24/40; $P=0.36$). No difference between phases was detected in neurodevelopment measured in the infant cases and controls. Among FAS/PFAS cases in phase three, levels of moderate or severe depression were higher than among cases in phase one.

The intervention reached a large proportion of the population who recalled receiving information about FASD from nurses (81.3%, 52/64) and the media (60.7%, 34/56). Levels of maternal awareness about alcohol harms increased, with odds of correct knowledge 5.8–10.3 higher in phase three than phase one. When changes in awareness were examined separately by town, differences were detected in all these measures in De Aar, but few were detected in Upington, though all changes were in the same direction of effect. Some changes were detected in drinking attitudes and the giving of alcohol to children. Importantly, 74% (83/112) of women believed that using posters to communicate information about drinking harms could modify women’s drinking.

Table 2. Association between infant and maternal characteristics before and after a universal FASD prevention intervention in Northern Cape, South Africa

Variable group	Category (%)	Before intervention	After intervention	P-value
Infant outcomes in whole population				
FAS/PFAS	No FAS/PFAS	737/809 (91.1)	708/751 (94.3)	0.02
	PFAS	40/809 (4.9)	18/751 (2.4)	
	FAS	32/809 (4.0)	25/751 (3.3)	
Dysmorphology	All participants: median score (IQR), <i>n</i>	4 (2–7), 809	3 (1–6), 751	0.002 ^a
	FAS/PFAS: median score (IQR), <i>n</i>	13 (10–16), 72	14 (11–17), 43	0.31 ^a
Birth weight	Mean kilogram (sd), <i>n</i>	2.9 (0.55), 685	2.9 (0.54), 643	0.89 ^b
Infant anthropometry Z scores for age, median (IQR), <i>n</i>	Weight	−0.84 (−1.75 to −0.03) 779	−0.57 (−1.47 to −0.27) 711	<0.001 ^a
	Weight for length	−0.44 (−1.31 to 0.21) 778	0.06 (−0.87 to 0.87) 710	<0.001 ^a
	Length	−0.80 (−1.76 to −0.06) 783	−1.18 (−2.05 to −0.3) 712	<0.001 ^a
	Head circumference	0.2 (−0.57 to 0.88) 783	0.2 (−0.49 to 0.95) 712	0.40 ^a
Neurodevelopment in cases and controls				
Neuro-development ^c	Mental retardation or borderline (0–84)	22/125 (17.6)	13/55 (23.6)	0.40
	Below average (85–89)	13/125 (10.4)	7/55 (12.7)	
	Average (90–109)	71/125 (56.8)	23/55 (41.8)	
	Above average (110–119)	12/125 (9.6)	9/55 (16.4)	
	Superior (≥120)	7/125 (5.6)	3/55 (5.5)	
Maternal outcomes in cases and controls				
Alcohol use in pregnancy ^c	Never	48/106 (45.3)	23/57 (40.4)	0.39
	1 week each month of pregnancy	10/106 (9.4)	7/57 (12.3)	
	2–3 weeks each month of pregnancy	16/106 (15.1)	14/57 (24.6)	
	Every week in pregnancy	32/106 (30.2)	13/57 (22.8)	
	Median units/week (IQR), <i>n</i>	12.1 (4.4–26.5), 55	8.5 (4.4–16.0), 30	0.32
Knowledge about harms of drinking in pregnancy ^c	One drink in pregnancy harms fetus	57/106 (53.8)	60/65 (92.3)	<0.001
	Five drinks on one occasion in pregnancy harms fetus	57/105 (54.3)	57/63 (90.5)	<0.001
	Fine drinks everyday in pregnancy harms fetus	54/104 (51.9)	56/65 (86.2)	<0.001
Alcohol and children ^c	Gives the child alcohol to drink	10/103 (9.7)	2/65 (3.1)	0.10
Study intervention in cases and controls				
Exposure to FASD information ^c	Information from nurses	78/117 (66.7)	52/64 (81.3)	0.04
	Information from radio or TV	30/76 (39.5)	34/56 (60.7)	0.02
Perceptions of drinking modifiability ^c	Posters of harms of drinking during pregnancy would alter alcohol use	43/66 (65.2)	40/46 (87.0)	0.01

Data are *n/N (%)* and χ^2 test unless indicated.

IQR, inter-quartile range; FASD, fetal alcohol spectrum disorder; FAS, fetal alcohol syndrome; PFAS, partial fetal alcohol syndrome.

^aMann–Whitney *U*-test.

^bStudent’s *t*-test.

^cData on cases and controls, not the whole population.

Table 3. Multivariate logistic regression of factors associated with FASDs in Northern Cape, South Africa

Study variable	Univariate odds of FAS/ PFAS (95% CI)	Adjusted odds of FAS/ PFAS (95% CI)
Study phase		
Before intervention	1	1
After intervention	0.62 (0.42–0.92)	0.73 (0.58–0.91)
Site		
Upington	1	1
De Aar	2.13 (1.44–3.17)	2.40 (1.54–3.74)
Maternal age (years)		
15–19	1	1
20–24	0.85 (0.25–2.86)	0.79 (0.23–2.67)
25–29	2.57 (0.85–7.75)	2.42 (0.80–7.33)
30–34	6.83 (2.34–19.89)	6.26 (2.17–18.03)
35–60	10.36 (3.46–30.98)	11.04 (3.79–32.16)
Ethnicity		
Black or other	1	1
Mixed ancestry	3.79 (1.82–7.90)	4.05 (1.91–8.63)

FAS/PFAS, fetal alcohol syndrome and partial fetal alcohol syndrome; CI, confidence interval.

No change, however, was noted in tobacco use during pregnancy, which remained above 50% in both phases.

Factors associated with FAS/PFAS

Maternal characteristics of children with FAS/PFAS are markedly different from that of the whole population (Table 1, comparing columns A and B with C and D). Most notably, in FAS/PFAS cases, maternal age and parity are substantially higher; women were more likely to be single or cohabiting; maternal educational attainment was lower and two-thirds of these mothers are affected by depression (59/91, 65%). Of 103 FAS/PFAS cases, 36 mothers were aged above 35 years and a further 37 were 30–34 years; together 70.9% of all FAS/PFAS cases were born to women above 30. In multivariate analysis, a stepwise increase in odds of FAS/PFAS was noted with each 5-year increase in age category beyond 25 years. Women of mixed ancestry were 4.05-fold more likely to have a FAS/PFAS child than other women (95%CI AOR = 1.91–8.63). Finally, FAS/PFAS was 2.4 times more likely in De Aar than in Upington (95% CI AOR = 1.54–3.74).

DISCUSSION

Although it is generally recommended that programs to prevent FASD should include universal or community-level measures (Floyd *et al.*, 2009), little has been done to document their effectiveness. The study, albeit in the absence of external controls, found a reduction in FAS/PFAS following CHW-led community- and facility-level interventions to shift drinking norms. Women in phase three had a higher knowledge of the harms of alcohol in pregnancy, and most had been exposed to FASD educational media and believed that these would modify their drinking behaviours. Taken together, these findings provide supportive evidence of the need for enhanced community-level interventions in settings

where levels of knowledge about the harms of maternal drinking are low. Further, operationally, CHWs, working with supervision, appear to be effective mediators for such interventions. Levels of FASD pre-intervention (112.8/1000 in De Aar and 65.9/1000 in Upington) were broadly comparable to a previous survey of school-entry children (119.4/1000 in De Aar and 74.7/1000 in Upington). Slight differences between these levels might be ascribed to reduced ability to detect neurobehavioral manifestations of FASD in young children. Though FASD was substantially lower in the post-intervention cohorts, levels remain unacceptably high.

There are few FASD prevention trials to date and the limited data mainly concerns selective interventions during pregnancy (Stade *et al.*, 2009). The study findings, however, concur with overall evidence of the effectiveness of alcohol-reduction interventions. There is much evidence that brief educational or motivational interventions are effective in reducing risky drinking (Moyer *et al.*, 2002; Kaner *et al.*, 2007), across a range of settings (including primary or antenatal health care). Even minimal interventions, such as those provided to control groups in randomized trials, may substantially reduce alcohol consumption (Aalto *et al.*, 2000; O'Connor and Whaley, 2007). We contend that our finding of an association between universal interventions and reduced FASD levels is consistent with this evidence of the modifiability of drinking, even through limited interventions.

Diagnosis of FAS/PFAS is multifaceted and the FAS phenotype evolves over time (Gibbard *et al.*, 2003; National Center on Birth Defects and Developmental Disabilities *et al.*, 2004; Davies L *et al.*, 2011). FASD surveys in South Africa have frequently targeted school-entry children, since the diagnosis is believed to be most easily and accurately made at this age. Nevertheless, FASD guidelines provide for the diagnosis to be made from early in life (Hoyme *et al.*, 2005), which enables early entry of affected children into services to improve their neurodevelopment (Bertrand, 2009) and also allows timely evaluation of outcomes of FASD prevention studies. The early diagnosis of FASD does, however, make it difficult to detect more subtle neurological manifestations of FASD, such as ARND.

A randomised trial among heavy-drinking women reported birth outcomes (weight, length and head circumference) (O'Connor and Whaley, 2007). That trial found that women allocated to a brief intervention had newborns of greater length and birth weight than controls. In our study among the general population, we did not find consistent population-level differences in infant anthropometry, but did detect population-level differences in dysmorphology scores.

The finding that PFAS levels and the volume of alcohol drunk among women with a PFAS infant had decreased to a greater extent than with FAS may be explained by an inability of universal interventions to modify drinking behaviours in women with entrenched heavy drinking or alcohol dependence. Similarly, these interventions may be less effective in women with depression. While universal interventions are well suited to altering occasional episodic drinking in pregnancy, alcohol-dependent women and those with depression require more individualized and specialized services to alter their drinking (WHO, 2001b).

Presently there are initiatives to enhance the role of CHWs in South Africa (Clarke M *et al.*, 2008). There are, however,

challenges in translating CHW-led interventions from research to routine practice environments (Lehmann and Sanders, 2007; Clarke M *et al.*, 2008), and within routine services CHWs would require ongoing supervision and monitoring, as in this study. The study also found that nurses were an important source of information regarding FASD, and the most frequently quoted source of information. This is important given that low levels of FASD knowledge among health providers remains a persistent problem globally (National Center on Birth Defects and Developmental Disabilities *et al.*, 2004; Brems *et al.*, 2010).

Aside from exposure to the study intervention, several other variables were strongly associated with FAS/PFAS occurrence, and similar to the previously identified factors (Morojele *et al.*, 2010). Identification of risk factors allows for future studies of selective interventions that target high-risk groups. For example, FAS/PFAS occurred in a fifth of children born to women of mixed ancestry and above 35 years.

Study strengths and limitations

The study is strengthened by having clinical outcome criteria such as FAS/PFAS and population-level dysmorphology scores rather than proxy criteria, as in previous studies. Measures of self-reported drinking likely incurred substantial social-desirability bias, especially post-intervention when awareness of the harms of maternal drinking increased. The study design makes it difficult to attribute the reduction in FAS/PFAS prevalence to the intervention alone, as concurrent changes in the community might account for these effects, even in part. However, the lack of change in tobacco use and employment status, as well as evidence of an increase in FASD in South Africa (discussed in introduction) suggest that temporal changes do not account for all the effects noted in this study. National programs for reducing alcohol use are poorly developed in South Africa and are unlikely to have interfered with our intervention. A more robust experimental study design was deemed unfeasible given the limited study resources available. Nevertheless, the weak design limits the ability to draw firm inferences. Further, collecting information on only the mothers of controls and cases reduced the ability to detect differences between women's behaviours in phases one and three. The absence of data on the participation rates for two of the four cohorts should be noted, this information is important for judging the likelihood of selection bias. Data are also missing for other study variables, mostly due to incomplete information in the multiple data sources used.

Effectiveness of the interventions may be reduced within larger or more transient populations, or where knowledge about the harms of drinking during pregnancy is already high. Low FASD knowledge levels have, however, been documented in several other South African settings (May *et al.*, 2005, 2008; Morojele *et al.*, 2006).

CONCLUSIONS

This study provides information about the effectiveness of universal prevention of FASD in two South African towns, and suggests that in these and similar communities,

concerted efforts to increase awareness about the harms of drinking during pregnancy might lower FASD prevalence. However, even after the intervention, FASD prevalence is extraordinarily high, similar to that of paediatric human immunodeficiency virus infection levels in South Africa; a condition that elicits a markedly higher, yet appropriate, preventive response. Poor socio-economic indicators and frequent unintended pregnancies make intersectoral or structural interventions necessary. In the meantime, markedly increased efforts are needed to alter community norms about drinking in pregnancy, together with selective interventions for high-risk women and alcohol treatment services for women with alcohol dependence.

Funding — This work was supported by the Centers for Diseases Control and Prevention (CDC), the TransNet Foundation and a local benefactor. The alcohol industry's Association for Responsible Alcohol Use (ARA) provided financial support for study administration, but had no input into study activities, data analysis or the decision to publish the findings.

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