Regarding a call to action on the prevention of fetal alcohol spectrum disorder

To the Editor: We refer to the recent comments by Patel *et al*.[1] on the prevention of fetal alcohol syndrome (FAS), and the need for a guideline for the prevention and management of this major problem.[2] We appreciate their concern about FAS and their serious desire to address it. However, drinking during pregnancy should not be addressed in isolation, as the adverse effects go hand in hand with those of cigarette smoking and the use of other recreational drugs. The Safe Passage Study (SPS)[3] investigated the effects of drinking and smoking on the outcome of pregnancy in a large international prospective study on pregnant women, including in Cape Town, South Africa (SA).[3]

In the study of 11 663 pregnancies, the risk of stillbirth was almost twice as high when women smoked, but almost four times higher when they both drank and smoked.[4] In a study of 11 892 pregnancies, drinking by the mother during pregnancy did not increase the risk of an infant death from a known cause, in contrast with smoking, where the risk increased almost three times. Drinking did not increase the risk of sudden infant death syndrome (SIDS), but smoking increased the risk more than six times, and concomitant use almost 15 times.[5]

As increased impedance to flow in the uterine and umbilical arteries during early pregnancy are reliable indicators of maternal vascular underperfusion (placental insufficiency), we examined the Doppler flow velocity waveforms in these vessels in 5 806 pregnancies from the SA arm of the SPS, which demonstrated that impedance to flow in the uterine artery was significantly higher when women were heavy drinkers and smokers. Impedance in the umbilical artery was significantly higher even in mild drinkers and smokers. In contrast, neither drinking only nor smoking only had any significant effect on impedance to flow.[6]

Placental abruption was the most common cause of stillbirth in the SPS.[4] Further analyses of the 5 806 pregnancies in the SA arm demonstrated that the prevalence of early placental abruption was 0.11% in the 875 women who did not drink or smoke, but 1.25% in the 2 804 women who had used the two substances mildly, another indication of the synergistic effect of concomitant drinking and smoking on pregnancy outcome.[6]

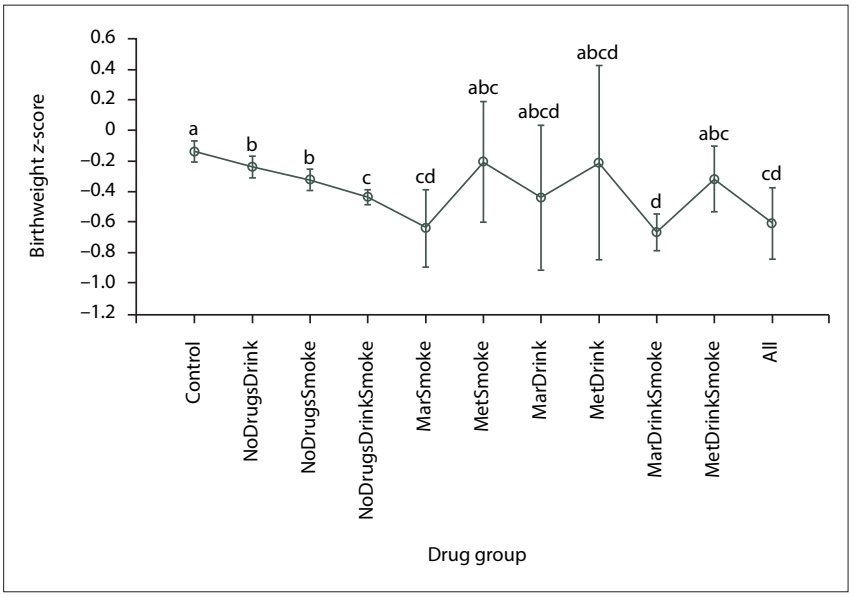

Fig. 1. The effects of different combinations of drug use on birthweight z*-scores. Birthweight* z*-score compared among different substance use groups (least-square means). Vertical bars denote 95% confidence intervals. Current effect: F(10, 4 836)=9.5572,* p*<0.01. Kruskal-Wallis* p*<0.01. Effective hypothesis decomposition. Birthweight* z*-score differs significantly between any two groups when there is no overlap of letters above the vertical bars. (Mar = marijuana; Met = methamphetamine.)*[7]

Exposure to various recreational drugs further jeopardises pregnancy, as reflected by their effects on birthweight *z*-scores (Fig. 1).[7]

Birthweight *z*-scores were significantly lower when women drank and smoked when compared with those who either drank only or smoked only. In addition, the lowest birthweight *z*-scores were seen in newborns where the mothers smoked marijuana and cigarettes, or used both substances and were also drinking.

In conclusion, as there seems to be a synergistic effect between drinking and smoking in many outcomes, it is likely that smoking may influence development of FAS, and in particular, cognitive aspects of FAS disorders. Prevention programmes on drinking should therefore also address cigarette smoking and the use of drugs in pregnancy in a comprehensive programme.

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Response to correspondence regarding a call to action on the prevention of fetal alcohol spectrum disorder

To the Editor: We thank Profs H Odendaal and H C Kinney for their thoughtful letter regarding our publication in the *SAMJ* titled 'Where is the South African prevention of fetal alcohol spectrum disorder programme? A call to action'.[1] Additionally, we appreciate the continued conversation regarding neglected aspects of maternal and child health.

The letter refers to the additive effects of concurrent smoking and alcohol use, as well as the independent effects of smoking during pregnancy, demonstrated in the Safe Passage Study (SPS) by the Prenatal Alcohol in Sudden infant death syndrome and Stillbirth (PASS) Network. This large longitudinal prospectively enrolled study in Cape Town (59% of the cohort) and the USA highlights significant and devastating consequences of alcohol and smoking in pregnancy. The primary outcomes described in the letter include stillbirths and sudden infant death syndrome (SIDS).[2] However, other adverse birth outcomes such as prematurity, low birthweight, infant death and longer-term effects on growth and wellbeing were also measured.[3,4]

We appreciate the strength of the Safe Passage Study and the importance of the data derived from it in a South African setting where substance use in pregnancy is prevalent. We agree with the professors that the evidence that smoking alone and in combination with alcohol use in pregnancy can result in adverse outcomes measured at birth and early life. Without detracting attention from the importance of these early life events, we highlight fetal alcohol spectrum disorder (FASD) effects throughout the life of the affected person. Owing to the nature of FASD, symptoms may be subtle, and present later in life, or be severe with long-term morbidity and a lifetime of challenges. Longer-term follow-up of the children in the SPS study may yet reveal further insights into the effects of alcohol use in pregnancy.

Alcohol use in pregnancy and FASD are complex, multifaceted issues. Socioeconomic, mental health and behavioural challenges, including addiction, contribute to continued alcohol use. Additionally, alcohol use may occur in isolation, but may also be accompanied by use of multiple recreational substances, often across generations. As substance-use risk factors and treatment strategies frequently overlap, management should be addressed holistically, incorporating education, nutritional support, psychosocial services, especially focusing on maternal mental health, and addiction-related therapies as part of broader harm-reduction approaches.

Prevention strategies should ideally be implemented before pregnancy. Once substance use occurs in pregnancy, effective reduction and, ideally, early cessation require a multidisciplinary approach to prevent adverse maternal, pregnancy and infant outcomes. The aspects we highlighted for FASD (societal education and awareness, prevention of unplanned pregnancies, early pregnancy detection and antenatal education and counselling) are not only relevant to alcohol use, but can be extrapolated to all substance use in pregnancy.

The importance of the availability of safe contraception options, preconception care and early pregnancy recognition cannot be understated. As a country, we have not yet shifted from a narrow focus on preventing unintended pregnancies to a broader emphasis on promoting safer conception. A paradigm shift is needed, both among women and within the healthcare system.

Safer conception enables early identification and mitigation of risks before pregnancy. It supports holistic preparation for pregnancy, including addressing alcohol and smoking, screening for infections and managing existing maternal conditions. To achieve this, we must evolve beyond traditional family planning services, and move toward a model centred on women's overall health and wellbeing.

Early pregnancy recognition and easy access to testing are also important. There are several models that could be explored, including:

(*i*) incorporating pregnancy testing as a routine vital sign for all women of reproductive age, enabling immediate initiation of antenatal care when pregnancy is confirmed

(*ii*) utilising community health workers to conduct pregnancy testing during household visits

(*iii*) integrating pregnancy self-testing into the broader package of women's health self-care interventions, ensuring that women can test easily, privately and at their convenience. This will need a monitored means of linking the women to care upon pregnancy confirmation.

The key questions remain: (*i*) how do we shift the narrative so that women are educated, empowered and supported to plan pregnancies, improve maternal health and reduce exposures to harmful substances prior to conception, identify pregnancies early and initiate antenatal care soon after recognition; and (*ii*) how do we develop and eventually integrate a comprehensive women-centred model of care into our resource-limited health system?

The answers lie in close collaboration, dialogue and interventions co-created with women, communities, healthcare workers, researchers, policy-makers, government departments and, dare we say, manufacturers of harmful substances.

In conclusion, we agree that the risk factors for alcohol, tobacco and recreational drug exposure during pregnancy overlap significantly, and their synergistic adverse effects impact pregnancy, birth outcomes and the long-term health of the child. A collaborative, comprehensive prevention programme – supported across sectors and integrated into standard care – is essential to improving maternal and child health.

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