further: all participants should receive the highest standard of care including quality referrals, support, treatment, and care.

Underlying these issues is the most profound problem with this trial: the lack of proper community involvement in its design. The IDU community in Thailand is not invisible: the Thai Drug Users Network has been in existence since 2002 and includes more than 120 members. But this group was not consulted at any stage.

According to the US Centers for Disease Control and Prevention, a community advisory board is planned, but only after the final protocol has been approved by three ethics committees. This would preclude community input in the study design and give little possibility for influencing the final protocol in any significant way.

The IDU community would like to support this trial. But community involvement must be a partnership based on reciprocity, not an a-posteriori response to bad publicity. Many in the IDU community in Thailand have legitimate concerns about the trial design and location, and are affronted that these concerns³ have been ignored. As a result, dialogue between the two sides has broken down.

This is not the first time HIV trials in Thailand have raised concerns from the community. Calls have previously been made for an institutional mechanism that would systematically ensure community participation, and steps have recently been taken to establish such a mechanism under the stewardship of the Thai Red Cross. A rigorous, standardised consultation process is the only way to ensure that trial participants in poorer countries are included as partners in international research. The tenofovir trial illustrates once again how urgently such a mechanism is needed.

We declare that we have no conflict of interest.

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On March 4, 2005, the Women's Network for Unity, a grassroots representative collective of sex workers based in Phnom Penh, Cambodia, wrote to Prime Minister Hun Sen about the tenofovir trials¹ in which they were to be recruited, stating: "Cambodian people are not waste and Cambodia is not waste bin!"

The Network has about 5000 members in 13 provinces and cities in Cambodia, yet was not consulted about the planning or implementation of the trial. The letter continues: "There are some NGOs still pushing women to participate in the unethical trial. Those people only think about their own benefit, not ours. They have not provided information and documents related to the trial to us . . . What worries us the most is that the research group does not have a clear ethics protocol for this clinical trial. They are pushing us to do what they think is right and take no concern about our lives."

It is worthy of note that there has been a reduction of new HIV cases for several years, attributed largely to the rising use of condoms in commercial sex.² However, sex workers' powerlessness and consequent vulnerability to HIV is made worse in Phnom Penh where almost all sex workers are raped, usually by police or gangsters who act with impunity because sex workers have no recourse to a justice system.

They are treated as non-citizens, without choice or rights. This is exemplified at times by the 100% Condom Use Programme which further deprives workers of control over their working environments.³ This reality, coupled with the nation's lack of quality medical services, makes current and future promises of medical treatment and negotiations for access to cheap tenofovir sound distressingly empty.

Duan has advocated a consumer model to counter barriers to participation in HIV vaccine trials.4 Sex workers, who have been subject to research for a couple of centuries with little discernable benefit to them, and often harm. would prefer not to be regarded as consumers of a research package. Sex workers have voices, as individuals and through groups formed to speak on their behalf, and expect to be part of the decision-making process about what research is done using their bodies, the design and implementation of this research, and subsequent follow-up. In the process carried out by researchers funded by the US National Institutes of Health, they were neither placed on the community advisory boards nor directly addressed about their concerns until after they had made such a fuss that the Prime Minister was forced to intervene.

Most generously, sex workers (and their advocates) have indicated their willingness to continue involvement in trials, but a great deal must change before researchers are worthy of their confidence. A political and social environment that undermines their status as human beings, and threatens their lives and wellbeing, must be relevant considerations when making decisions about research. And they must be party to this decision-making process from the earliest stages.

As people living at the margins, sex workers rarely have access to respectful treatment and thus are unlikely to derive benefits from the results of a trial in the long term—even were these to be promised. At the very least, they and their representatives should be treated with respect and their contributions



acknowledged in the context of research in which their very vulnerability makes them "ideal" participants.

We thank Andrew Hunter for his contribution to this letter.

We declare that we have no conflict of interest.

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Selective head cooling after neonatal encephalopathy

Peter Gluckman and colleagues' multicentre randomised trial on selective head cooling with mild systemic hypothermia after neonatal encephalopathy (Feb 19, p 663)¹ is a landmark study. However, a few points need clarification.

Why did Gluckman and colleagues not adjust for Apgar scores in the logistic regression analysis? The "cooled" group was at a disadvantage, since 70% had 10-min Apgar scores of 0–3, whereas only 55% in the control group had such scores. Apgar scores are clinically relevant with wide applicability and the difference was more stark than other parameters that were included in the regression analysis. Gluckman and colleagues had sufficient numbers to be able to include this variable in the regression model. Even if one argues that the independent variables for the

model had been decided a priori, surely Apgar scores should have been included up front.

We have also not been provided with data about antenatal events. Therefore it is difficult to judge whether or not some babies had intrauterine hypoxia and if so of what duration. If hypoxic damage had already occurred before birth, the postnatal head cooling would have been insufficient to prevent injury.

We declare that we have no conflict of interest.

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I Gluckman PD, Wyatt JS, Azzopardi D, et al, on behalf of the CoolCap Study Group. Selective head cooling with mild systemic hypothermia after neonatal encephalopathy: multicentre randomised trial. Lancet 2005; 365: 663-70.

Data from the study by Peter Gluckman and colleagues¹ on treatment of neonatal hypoxic ischaemic neonatal encephalopathy with head cooling reveal a reassuring unadjusted odds ratio of 0.61 (95% CI 0.34-1.09). However, the window for intervention and the management options in this disorder are quite narrow.^{2,3} Data from studies on such illnesses may require assessment beyond statistical significance. The wide confidence intervals in Gluckman and colleagues' study might suggest statistical insignificance, but they also reveal that the treatment could reduce the risk of the endpoints under consideration by as much as 66% or increase the risk by only 9%. The treatment effect after adjustment is even more reassuring (0.57, 0.32-1.01) and suggests essentially no risk from the treatment. Also, given the nature of the illness, an α level of 0.05 may have been too conservative.

Predetermined subgroup analysis might not have been a good idea in this study because it is intuitive that hypothermia could act by at least decelerating damaging inflammatory responses than it does more favourable responses and that this influence could be absent in severe injuries. During intervention, this intuition could have introduced bias against patients with more severe abnormalities on amplitudeintegrated electroencephalography (aEEG). A post-hoc subgrouping and analysis might have controlled such potential bias. Taken as they stand, the data still reveal a potential 51% reduction in risk in the more compromised neonates (1.8, 0.49-6.4). This finding is quite reassuring considering that the right side of the risk (6.4-fold increase) is not inconsistent with the risk from no intervention.

Overall, the result of the study suggests a potentially clinically important benefit of head cooling in neonatal hypoxic-ischaemic encephalopathy as a group, and could be of high clinical usefulness in developing economies where neonatal hypoxic-ischaemic encephalopathy is more common⁴ and where aEEG might not be available but head cooling could be feasible.

I declare that I have no conflict of interest.

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Authors' reply

As Sourabh Dutta and colleagues note, we saw a chance bias in randomisation so that more infants in the treatment group than the comparison group showed a very low 5-min Apgar score.

