Filtered Sunlight for Treatment of Neonatal Hyperbilirubinemia: A Rejoinder

We note the interest generated in this journal [1], on our paper [2], and wish to provide the following clarifications for the benefit of the readership. Dr. Mathew's opinion was that our study had a high risk of bias principally because: (*i*) specific method used for the sequence generation was unclear; (*ii*) the primary outcome (rate of bilirubin decline) assessors were not blinded; and (*iii*) 'treatment days', rather than 'number of infants enrolled' was chosen as unit of measurement.

First, Dr Matthew apparently overlooked details provided in our study protocol on the computer-generated block randomization done independently by the USA-based study statistician (provided as supplementary data to the main article [2]. The randomization method was indeed 'adequate' [3]. Second, as in most clinical settings, bilirubin levels were objectively determined by the laboratory technician using duly calibrated bilirubinometer on blood samples from the infants at stated intervals to monitor need for continuation or withdrawal of treatment by filtered sunlight or conventional phototherapy. As reported [2,4], the laboratory technician responsible for measuring serum bilirubin levels was unaware of the treatment allocation sequence prior to bilirubin determination for eligible infants. As our primary outcome was objectively measured and the risk of bias minimal, blinding of the participating parents, or the hospital personnel was considered unnecessary [2,3,5]. Third, the stated aim was to compare the rate of bilirubin decline in babies able to tolerate filtered sunlight or conventional phototherapy for at least 5 hours. As interruptions in the management of temperatures outside the acceptable range were not predetermined, treatment days were variable. Hence, the need to appropriately define the unit of measurement as a 'treatment day' rather than 'number of infants' randomized. This formed the basis of the required sample size. There was indeed no statistical or ethical justification for continuing with enrolment once the required treatment days had been achieved.

Finally, available evidence suggests that mothers and care-givers, with or without active support from health care providers will continue to expose their jaundiced infants to sunlight [6]. The duty of care, especially in populations with excessive rates of avoidable bilirubin encephalopathy [7], should compel care-providers to explore safe and efficacious means of applying filtered sunlight where conventional phototherapy cannot be readily assured. This is the overarching message and merit of our novel study. Appropriate adaptions should follow in earnest, to optimize the benefit of this low-cost, low maintenance and readily available intervention, wherever possible.

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Author's Reply

1. The trial protocol (Contents page), in the supplementary data [1] states that the Randomization procedure is presented in Section 5.2 on page 23; however Section 5.2 described Laboratory procedures (and not Randomization). The trial protocol published in the journal 'Trials' [2] also does not describe the random sequence generation process; it only states: "A block randomization

procedure with variable block sizes will be used to maximize unpredictability". Thus, as pointed out in the Commentary [3], the procedure used to generate the randomization sequence is 'unclear'.

2. The authors' assertion: "computer-generated block randomization done independently by the USA based study statistician" is not found either in the Supplementary data [1] or the published trial protocol [2]. The published paper [1] states that the external statistician performed allocation concealment (and not random sequence generation). The Commentary [3] already reported that allocation concealment was adequate.
3. The supplementary data [1] (Contents page) states that Blinding is described in Section 5.3 on page 23; however this section is missing in the text. The published protocol [2] states "TSB will be estimated using standard methods" without commenting on blinding. Thus it does not appear that blinding of the outcome assessor was done, hence it was described as 'Inadequate' [3]. Although many randomized trials cannot (and need not) include blinding of outcome assessors, the importance in this trial has already been highlighted previously [3].
4. The Supplementary data [1] and published protocol [2] have two different sample size calculations. The former describes a sample size of 124 infants (days of phototherapy not mentioned), whereas the latter describes the sample size as 560 treatment days. Neither affects the assessment that there is lack of clarity for information provided on the number of infants in the safety analysis [3]. It is important to note that this criterion has to be evaluated in trials for each outcome.
5. What can we learn (and apply) from this trial? Filtered sunlight could be efficacious for mild(er) neonatal jaundice (recall that the threshold was 3 mg/dL lower than standard practice) and can be used if (*i*) intensive monitoring is performed (as in the trial) and (*ii*) adequate backup phototherapy units are available (as about 1 in 7 babies would require phototherapy). Unfortunately, the trial does not explore whether we can predict which babies will require phototherapy, making it necessary to have back-up arrangements.

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Is Newborn Hearing Screening Worthwhile in India?

We congratulate and appreciate Dr Paul for setting up a newborn hearing screening program in Kerala, and reporting about it [1]. If it has to be replicated in other areas of the country a few more details are needed. Is the charge of Rs 150 per child, a one-time payment, and does it cover repeat tests in those who need it. Was the program supported by any grant?

The author had screened 1,01,688 babies, out of which 15123 failed the first test and of these 1,634 babies failed the second screen. Finally, deafness was diagnosed in 162. Assuming no further charges were made for repeat tests, the cost of detecting one case of deafness works out to be approximately Rs. 100,000. In addition, unnecessary anxiety may be caused to 15% of the mothers who were informed that their child had failed the hearing test initially.

Only profound hearing defects are picked up by these screening tests. The author states that hearing loss must be detected before 6 months of age. Most mothers would easily pick up the cues of lack of responsiveness to sound before the child reaches the age of 6 months. One wonders if this screen is really useful and cost-effective in India.

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