

ORIGINAL ARTICLE

A Randomized Trial of Phototherapy with Filtered Sunlight in African Neonates

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ABSTRACT

BACKGROUND

Sequelae of severe neonatal hyperbilirubinemia constitute a substantial disease burden in areas where effective conventional phototherapy is unavailable. We previously found that the use of filtered sunlight for the purpose of phototherapy is a safe and efficacious method for reducing total bilirubin. However, its relative safety and efficacy as compared with conventional phototherapy are unknown.

METHODS

We conducted a randomized, controlled noninferiority trial in which filtered sunlight was compared with conventional phototherapy for the treatment of hyperbilirubinemia in term and late-preterm neonates in a large, urban Nigerian maternity hospital. The primary end point was efficacy, which was defined as a rate of increase in total serum bilirubin of less than 0.2 mg per deciliter per hour for infants up to 72 hours of age or a decrease in total serum bilirubin for infants older than 72 hours of age who received at least 5 hours of phototherapy; we prespecified a noninferiority margin of 10% for the difference in efficacy rates between groups. The need for an exchange transfusion was a secondary end point. We also assessed safety, which was defined as the absence of the need to withdraw therapy because of hyperthermia, hypothermia, dehydration, or sunburn.

RESULTS

We enrolled 447 infants and randomly assigned 224 to filtered sunlight and 223 to conventional phototherapy. Filtered sunlight was efficacious on 93% of treatment days that could be evaluated, as compared with 90% for conventional phototherapy, and had a higher mean level of irradiance (40 vs. 17 μ W per square centimeter per nanometer, $P < 0.001$). Temperatures higher than 38.0°C occurred in 5% of the infants receiving filtered sunlight and in 1% of those receiving conventional phototherapy ($P < 0.001$), but no infant met the criteria for withdrawal from the study for reasons of safety or required an exchange transfusion.

CONCLUSIONS

Filtered sunlight was noninferior to conventional phototherapy for the treatment of neonatal hyperbilirubinemia and did not result in any study withdrawals for reasons of safety. (Funded by the Thrasher Research Fund, Salt Lake City, and the National Center for Advancing Translational Sciences of the National Institutes of Health; Clinical Trials.gov number, NCT01434810.)

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WORLDWIDE, SEVERE NEONATAL hyperbilirubinemia affects at least 481,000 term or near-term newborn infants annually, of whom 114,000 die and more than 63,000 survive with moderate or severe disabilities.¹⁻³ The majority of affected infants (>75%) reside in low-to-middle-income countries, particularly in sub-Saharan Africa.¹⁻⁵ Severe neonatal hyperbilirubinemia that progresses to acute bilirubin encephalopathy or kernicterus is devastating for infants, children, and their families, since surviving children may have severe long-term impairments, including choreoathetoid cerebral palsy, deafness, language-processing disorders, and general developmental delays.⁶⁻¹⁰ These outcomes are rare in high-income countries, where there is timely recognition of clinically significant hyperbilirubinemia and access to effective treatment with phototherapy.¹¹⁻¹³ Levels of bilirubin have long been known to be altered by light.¹⁴ Building on this knowledge, investigators developed modern phototherapy as the primary treatment for neonatal hyperbilirubinemia.¹⁵ However, in areas with limited resources, conventional phototherapy, defined as irradiance of at least 8 to 10 μ W per square centimeter per nanometer,¹⁶ is often unavailable because of its cost or ineffective because of the inconsistent supply of electrical power or the low levels of irradiance emitted by the phototherapy bulbs available, which may be inferior in quality or limited in quantity or may have deteriorated.¹⁷⁻²⁰

We previously reported the results of the initial phase of this study, in which phototherapy with filtered sunlight was found to be safe and efficacious when used to reduce excessive total serum bilirubin.²¹⁻²³ We now report the results of the second phase of the study, a randomized trial in which filtered sunlight is directly compared with conventional phototherapy.

METHODS

STUDY DESIGN

This randomized, controlled, nonblinded, non-inferiority trial was conducted at Island Maternity Hospital, a large inner-city hospital in Lagos, Nigeria, in accordance with our previously published protocol.²² We obtained approval from the institutional review boards and ethics committees of the University of Minnesota, the Minnesota Medical Research Foundation, and the Lagos

State Government. The light-filtering films used in the study were approved by the National Agency for Food and Drug Administration and Control of Nigeria and were donated by CPFilms, which had no other role in the study. The study protocol is available with the full text of this article at NEJM.org. The first and second authors take responsibility for the accuracy and completeness of reporting and the fidelity of the report to the protocol.

STUDY PROCEDURES

All infants who were up to 14 days of age and had a gestational age of least 35 weeks (or weighed >2.2 kg, if the gestational age was unknown) were eligible for participation. Although skin color varies widely, especially at birth, all infants in this study were black Africans. Infants in hospital were screened daily in accordance with routine hospital protocol, and infants who returned for evaluation of jaundice were also screened, with the use of the JM-103 transcutaneous bilirubinometer (Draeger Medical).²² If the transcutaneous bilirubin level was elevated, then total serum bilirubin was measured with the use of the Advanced BR2 Bilirubin Stat-Analyzer (Advanced Instruments). If the total serum bilirubin was elevated (as defined in our protocol), the infant was eligible for enrollment and treatment, and written informed consent was obtained from the parent or guardian. The screening and treatment thresholds for bilirubin levels (Table S1 in the Supplementary Appendix, available at NEJM.org) were 3 mg per deciliter lower than the guideline recommended by the American Academy of Pediatrics¹⁶ as a safety precaution, since filtered sunlight had not been used for this purpose previously and hemolysis resulting from a deficiency of glucose-6-phosphate dehydrogenase or from blood-group incompatibilities is common in Nigeria.²⁴

The exclusion criteria included the need for medical treatment elsewhere, a life expectancy of less than 24 hours, the need for oxygen therapy, clinical dehydration or sunburn, a temperature lower than 35.5°C or higher than 38.0°C, a diagnosis of acute bilirubin encephalopathy, or the need for exchange transfusion. Enrolled infants were randomly assigned to receive filtered sunlight or conventional phototherapy with the use of a block randomization procedure, with block sizes of 2, 4, 6, 8, and 10. Treatment as-



A Quick Take is available at NEJM.org

signments recorded on sequentially numbered sheets of paper, enclosed in opaque, sealed, matching, numbered envelopes, were shipped to Lagos and opened sequentially for each enrolled infant.

Laboratory tests included total serum bilirubin, hematocrit, maternal and infant blood grouping, and screening for glucose-6-phosphate dehydrogenase.²⁵ Irradiance was measured hourly outdoors and under a canopy that filtered sunlight and once daily under conventional phototherapy units with the use of the BiliBlanket Meter II (GE Healthcare), which has a wavelength sensitivity of 400 to 520 nm, with a peak sensitivity of 450 nm.

Total serum bilirubin was measured at the start and end of each treatment day, which was defined as at least 5 hours of phototherapy, generally from 10 a.m. to 4 p.m. Measurement of axillary body temperatures and a clinical evaluation for dehydration and sunburn were obtained hourly.

On the basis of data from our previous study,²³ hyperthermia was managed prophylactically with wet white towels placed under and, if needed, around the infant with temperatures higher than 37.5°C and up to 38.0°C and therapeutically with temperatures higher than 38.0°C with brief removal from phototherapy to a shaded area. Hypothermia (temperature <35.5°C) was managed by swaddling the infant in cloth briefly, by providing skin-to-skin care with the mother (also called kangaroo care), or both. Infants with temperatures higher than 38.0°C or lower than 35.5°C for more than 1 hour or higher than 39.0°C or lower than 35.0°C on two or more occasions, or who received treatment for sunburn or dehydration (excluding breast-feeding) met the criteria for study withdrawal. Additional criteria for withdrawal included the need for an exchange transfusion, the presence of an intercurrent illness incompatible with phototherapy, parental request, death, or hospital transfer. The protocol was completed when the infant's total serum bilirubin no longer met the criteria for study entry. Safety data were reviewed by the data and safety monitoring board at the midpoint of the study (June 2013).

INTERVENTIONS

Infants assigned to the group receiving filtered sunlight were placed under one of two previously

tested film canopies (donated by CPFilms) depending on whether the sky was overcast, in which case the Air Blue 80 film was used, or sunny, in which case Gila Titanium film was used. Infants were rotated between canopies as needed.²¹⁻²³ Both films filter out most ultraviolet A light (>99%), virtually all ultraviolet B and C light, and some infrared (heat) radiation while allowing passage of 84% (Air Blue 80) and 39% (Titanium) of therapeutic blue light (400 to 520 nm). Detailed characteristics of these films have been described.²¹⁻²³ Infants assigned to receive conventional phototherapy were placed under phototherapy constructed according to published specifications with the use of locally available materials,²⁶ with maintenance of irradiances of at least 8 to 10 μ W per square centimeter per nanometer^{27,28} (Fig. S1 in the Supplementary Appendix). The indication for the use of conventional nighttime phototherapy in both groups was an afternoon total serum bilirubin that was at least the treatment level for age-in-hours recommended by the American Academy of Pediatrics.

STUDY END POINTS

The primary end point was efficacy, with a noninferiority margin of 10%. The criteria for efficacy were unchanged from our previous study²³ and included a rate of increase in total serum bilirubin of less than 0.2 mg per deciliter per hour for infants up to 72 hours of age or a decrease in total serum bilirubin for infants older than 72 hours of age who were receiving at least 5 hours of phototherapy. These levels were chosen on the basis of expert consultation, the guideline from the American Academy of Pediatrics,¹⁶ and data from Johnson et al.²⁹ The secondary end point was the proportion of infants requiring exchange transfusion, with a noninferiority margin of 5%.

We followed the previously published safety protocol from the first phase of the study.²³ Phototherapy was deemed safe if an infant was able to receive phototherapy without meeting the study criteria for withdrawal for hyperthermia, hypothermia, dehydration, or sunburn.

SAMPLE SIZE

A total of 560 treatment days that could be evaluated was required to have 80% power for a test of noninferiority with a margin of 10%, assuming at least 5 hours of exposure to photo-

therapy on 90% of treatment days, with an average efficacy of 80%. Given a conservative estimate of the need for 1 day of phototherapy per infant, and with an estimated 40% of enrolled infants expected to go without treatment because their total serum bilirubin made them ineligible or because of rain or withdrawal of consent, we planned to enroll 924 infants.

STATISTICAL ANALYSIS

Study data were recorded on paper forms and then transferred to a secure, Web-based REDCap database.³⁰ Data cleaning and statistical analyses were carried out with the use of statistical software package R, version 3.1.1.

The following data were summarized: demographics, blood groups for mother–infant pairs, irradiance levels inside and outside filtered sunlight canopies and inside conventional phototherapy cots, and days of phototherapy received. Differences according to assigned treatment were tested with the use of Wilcoxon rank-sum tests for continuous variables and Pearson chi-square tests or exact binomial 95% confidence intervals for categorical variables. The safety and efficacy of filtered-sunlight and conventional phototherapy were compared on an intention-to-treat basis. Additional comparisons were planned on an as-treated basis for treatment actually received and on a per-protocol basis for infants receiving the assigned treatment on all treatment days. All treatment days were analyzed, including those days on which treatment was received by infants who were later withdrawn from the study. Safety was compared with the use of Fisher's exact test. Efficacy was compared with the use of one-sided chi-square tests of noninferiority with a prespecified margin of 10%.

Post hoc exploratory analyses of the effects of initial bilirubin level, average irradiance level, and treatment (filtered sunlight vs. conventional phototherapy) on bilirubin kinetics were conducted with the use of Wilcoxon rank-sum tests and general linear mixed models. The rate of change in total serum bilirubin was modeled as a linear function of initial bilirubin level, average irradiance level, and treatment group, with a random effect of the individual infant to account for potential correlation. Models were compared with the use of Akaike's information criterion without attempting to correct for multiple comparisons.

RESULTS

ENROLLMENT AND FOLLOW-UP

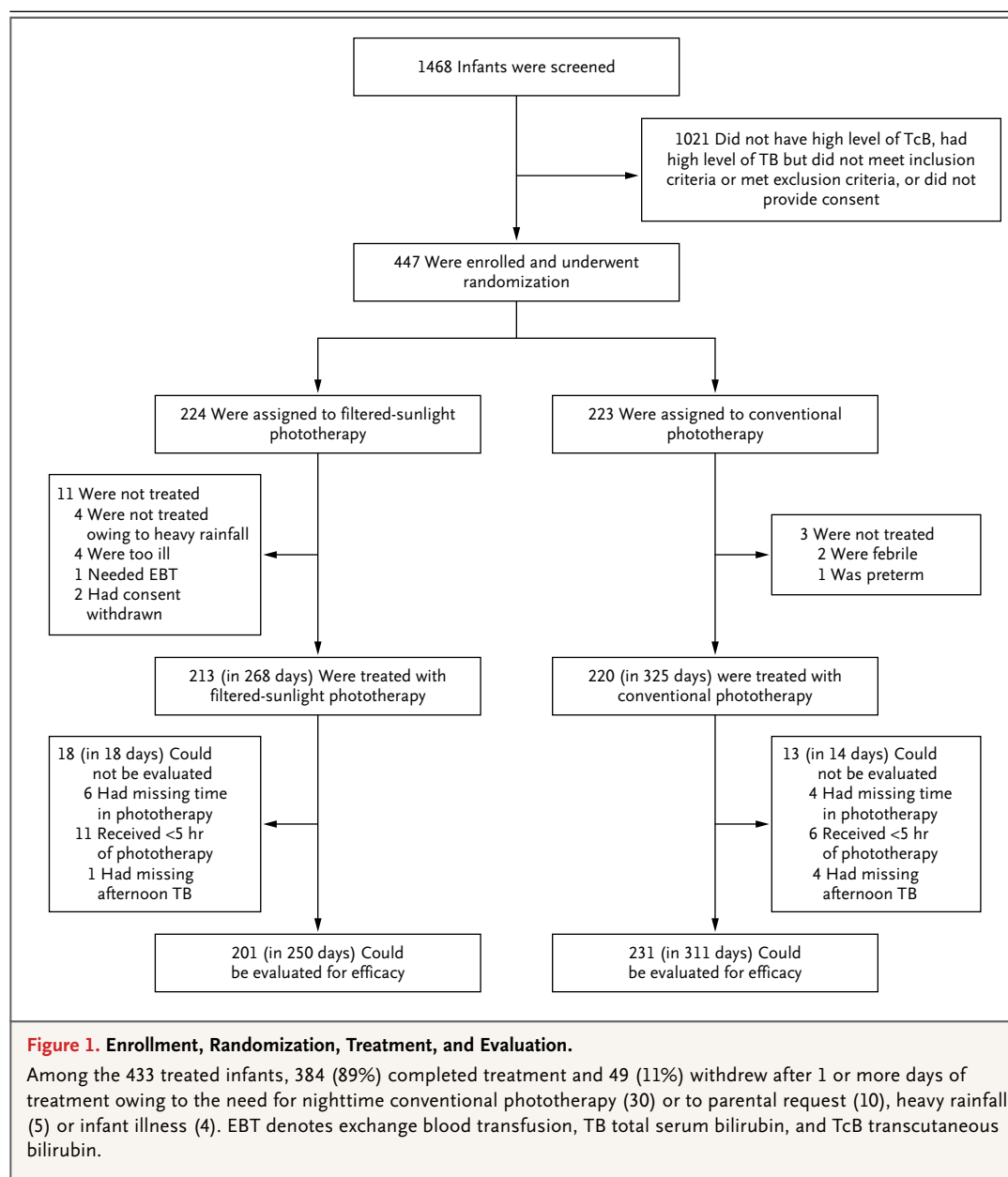
Between November 2012 and September 2013, a total of 1468 term and late-preterm infants were screened for jaundice with the use of transcutaneous bilirubinometry, in accordance with the protocol. Because of lower-than-anticipated rates of nontreatment and a higher-than-anticipated number of days required for phototherapy, we reached the required number of treatment days that could be evaluated (560 days) in 10 months with 447 eligible infants who were enrolled and randomly assigned to receive either filtered sunlight (224) or conventional phototherapy (223). Fourteen randomized infants (3%) did not receive phototherapy (Fig. 1). Of 433 treated infants, 384 (89%) completed treatment and 49 withdrew early. (Reasons for withdrawal are shown in Fig. 1.)

A total of 213 infants received 268 days of filtered-sunlight phototherapy, and 220 infants received 325 days of conventional phototherapy (Table S2 in the Supplementary Appendix). Only 5 infants required more than 4 days of phototherapy; all were in the conventional phototherapy group. Two mothers of infants receiving conventional phototherapy requested transfer to phototherapy with filtered sunlight on the last treatment day (day 6). Nighttime phototherapy for one night or more was indicated for 28 infants (13%) in the filtered-sunlight group and 35 infants (16%) in the conventional phototherapy group.

Safety was assessed for all 593 treatment days, and efficacy was assessed for the 561 days that could be evaluated (95%). Efficacy could not be evaluated for 32 treatment days because the phototherapy time was less than 5 hours (17 days), afternoon measurements of bilirubin were missing (5 days), or the data for phototherapy time were missing (10 days).

PARTICIPANT CHARACTERISTICS

The demographic and baseline characteristics of enrolled infants, including the results of laboratory analyses, are shown in Table 1. There were no significant differences between the filtered-sunlight and conventional phototherapy groups at baseline. Overall, 83 infants had glucose-6-phosphate deficiency, 76 were at risk for ABO incompatibility, and 13 were at risk for Rh incompatibility (Table 1).



IRRADIANCE MEASUREMENTS

The irradiance from filtered sunlight was measured 2959 times (with 88% of the measurements performed under the Air Blue 80 canopy and 12% under the Gila Titanium canopy), and the irradiance from conventional phototherapy was measured 293 times. Mean irradiance levels were significantly higher with filtered sunlight than with conventional phototherapy (40 vs. 17 μW per square centimeter per nanometer, $P < 0.001$). As expected, the spread of irradiances was much

wider for filtered sunlight than it was for conventional phototherapy (Fig. 2A), with highest irradiances occurring between noon and 2 p.m. (Fig. 2B).

EFFICACY

Filtered-sunlight phototherapy was efficacious on 93% of days that could be evaluated as compared with 90% for conventional phototherapy according to an intention-to-treat analysis (Table 2). As-treated and per-protocol analyses yielded sim-

Table 1. Baseline Characteristics of the Study Population.*

Characteristic	Filtered-Sunlight Phototherapy (N = 224)	Conventional Phototherapy (N = 223)
Male sex — no. (%)	122 (54)	120 (54)
Estimated gestational age — wk		
Median	38	38
Interquartile range	38–39	38–39
Birth weight — kg		
Median	3.2	3.2
Interquartile range	2.9–3.5	2.9–3.6
Hematocrit — %		
Median	53	55
Interquartile range	47–58	47–60
Initial total serum bilirubin on day 1 — mg/dl		
Median	5.9	6.2
Interquartile range	4.9–7.7	5.0–8.0
Infant's blood type — no./total no. (%)		
A	45/221 (20)	47/222 (21)
B	45/221 (20)	42/222 (19)
AB	6/221 (3)	6/222 (3)
O	103/221 (47)	110/222 (50)
Unknown	22/221 (10)	17/222 (8)
Mother's blood type — no./total no. (%)		
A	39/223 (17)	43/222 (19)
B	35/223 (16)	26/222 (12)
AB	4/223 (2)	3/222 (1)
O	110/223 (49)	110/222 (50)
Unknown	35/223 (16)	40/222 (18)
ABO incompatibility — no./total no. (%)		
No	135/221 (61)	123/221 (56)
Yes	34/221 (15)	42/221 (19)
Unknown	52/221 (24)	56/221 (25)
Infant's Rh status — no./total no. (%)		
Positive	186/222 (84)	191/222 (86)
Negative	13/222 (6)	14/222 (6)
Unknown	23/222 (10)	17/222 (8)
Mother's Rh status — no./total no. (%)		
Positive	175/224 (78)	173/222 (78)
Negative	12/224 (5)	9/222 (4)
Unknown	37/224 (17)	40/222 (18)
Rh incompatibility — no./total no. (%)		
No	160/222 (72)	160/221 (72)
Yes	8/222 (4)	5/221 (2)
Unknown	54/222 (24)	56/221 (25)
Glucose-6-phosphate dehydrogenase status — no./total no. (%)		
Present	184/224 (82)	169/221 (76)
Deficient	35/224 (16)	48/221 (22)
Unknown	5/224 (2)	4/221 (2)

* None of the between-group differences were significant at $P < 0.05$.

ilar results (efficacy, 93% vs. 90% in both cases). No infant in either group required an exchange transfusion.

SAFETY

No infant in either group met the criteria for withdrawal related to safety. Axillary temperature exceeded 39.0°C once, for 1 infant, but returned to the normal range within 25 minutes after the infant was moved to the shade and treated with wet towels. Axillary temperature exceeded 38.0°C in 5% of temperature checks in the filtered-sunlight group versus 1% in the conventional phototherapy group ($P < 0.001$) (Table 2, and Fig. S2 in the Supplementary Appendix). Axillary temperature exceeded 38.0°C in one or more measurements in 61 of the infants receiving filtered sunlight (29%) and 13 of those receiving conventional phototherapy (6%), and the temperature exceeded 38.0°C more than twice in 16 of the infants exposed to filtered sunlight (8%) and none of those exposed to conventional phototherapy. Wet white towels were used prophylactically or therapeutically for 68% of infants receiving filtered sunlight in 34% of the periodic checks versus 24% for those receiving conventional phototherapy in 7% of periodic checks. Hypothermia (axillary temperature, $< 35.5^{\circ}\text{C}$) occurred infrequently (8 of 1863 checks in the filtered-sunlight group vs. 2 of 2160 checks in the conventional phototherapy group [$P = 0.03$]) and was treated in accordance with the protocol, as noted earlier.

POST HOC EXPLORATORY ANALYSES

Total serum bilirubin fell more rapidly on treatment with filtered sunlight than with conventional phototherapy (Table 2). With filtered sunlight, the median rate of change in bilirubin was -0.07 mg per deciliter per hour, and with conventional phototherapy, the median rate of change was 0.00 mg per deciliter per hour ($P < 0.001$). Bilirubin levels fell significantly more rapidly when the initial (morning) bilirubin level was at least 12 mg per deciliter (Table S3 in the Supplementary Appendix) and on days when the average irradiance was at least $30 \mu\text{W}$ per square centimeter per nanometer (Table S3 in the Supplementary Appendix). Higher initial bilirubin levels, higher average irradiance, and filtered sunlight were all associated with a more rapid decline in bilirubin level (Table S4 in the Supplementary Appendix).

DISCUSSION

This randomized trial involving African neonates showed that phototherapy with filtered sunlight was safe and noninferior in efficacy as compared with conventional phototherapy, the standard treatment for neonatal hyperbilirubinemia. Both types of phototherapy were highly and similarly efficacious (93% of treatment days for filtered sunlight and 90% for conventional phototherapy).

Our original study showed that average irradiance levels delivered by filtered sunlight were above the threshold for intensive phototherapy (at least 30 μW per square centimeter per nanometer).^{16,28} A previous *in vitro* study conducted in the Middle East showed that sunlight was 6.5 times as effective as conventional phototherapy in isomerizing aqueous bilirubin solutions.³¹ Given the higher irradiance derived from sunlight than is used in conventional phototherapy, we hypothesized that filtered-sunlight phototherapy should be superior to conventional phototherapy in reducing bilirubin levels over time. The present trial was not designed as a superiority trial and did not include infants with bilirubin levels greater than 15 mg per deciliter.

In our trial, no infant required exchange transfusion or was withdrawn from treatment for reasons of safety. Little is known about the longer-term toxicity associated with brief exposures to high-intensity, broad-spectrum visible light, but some U.S. studies of phototherapy units have reported irradiance levels of up to 76 μW per square centimeter per nanometer.²⁸ A follow-up study of patients with the Crigler-Najjar syndrome who received lifelong treatment with nightly (8–10 hours), high-intensity (up to 100 μW per square centimeter per nanometer) phototherapy (>75,000 lifetime hours of high-intensity blue light) did not show any serious health consequences associated with this exposure.³² In our trial, phototherapy was of short duration — 5 to 6 hours per day for 1 to 2 days — for most infants. The risk of skin cancer was also low, since our films filtered out more than 99% of ultraviolet radiation. The development of films whose filtering characteristics automatically adjust in response to the intensity of sunlight (similar to light-sensitive lenses in eyeglasses) could provide more consistent levels of irradiance. From a practical perspective, especially in a developing country such as Nigeria, the theoretical

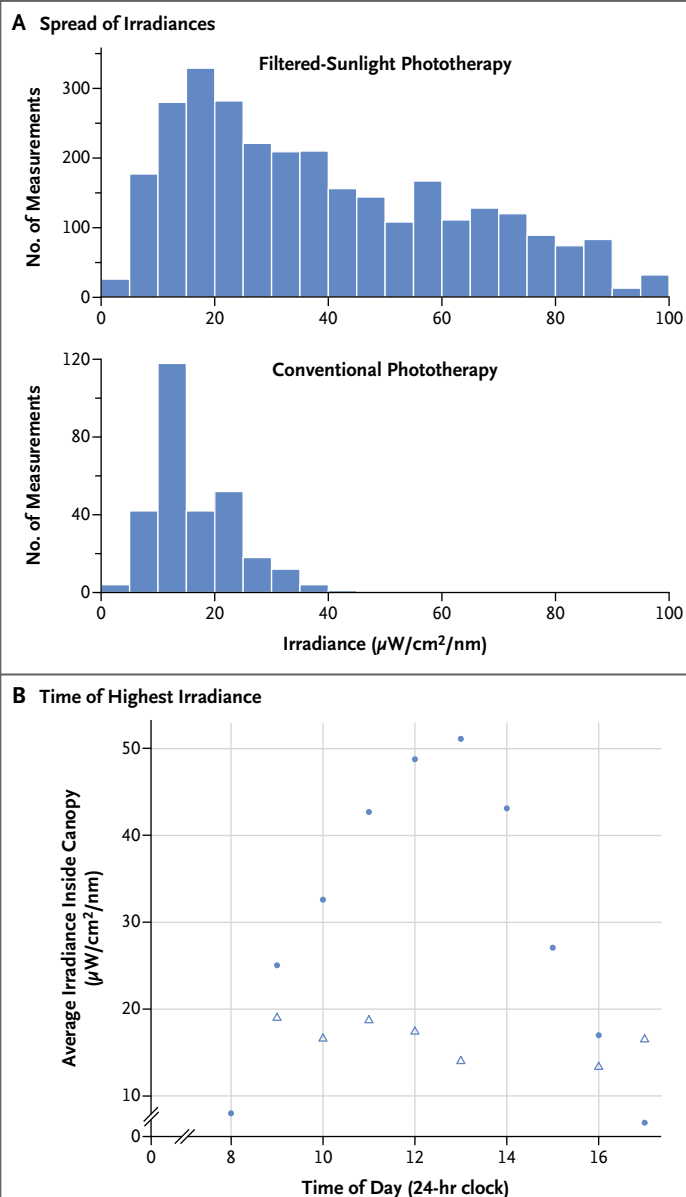


Figure 2. Spread of Irradiances and Time of Highest Irradiance for Filtered-Sunlight Phototherapy versus Conventional Phototherapy.

Panel A shows the measured canopy irradiances for infants assigned to filtered-sunlight phototherapy (upper graph) and conventional phototherapy (lower graph). Panel B shows the average canopy irradiance as a function of time of day for all treatment days for filtered-sunlight phototherapy (circles) and conventional phototherapy (triangles).

or unknown risks of brief exposures to high-intensity light must be weighed against the risk of death or severe disability associated with acute bilirubin encephalopathy and kernicterus.

Table 2. Efficacy and Safety.*

Variable	Filtered-Sunlight Phototherapy	Conventional Phototherapy
Efficacy		
Days treatment received — no.	268	325
Days that could be evaluated — no.†	250	311
Rate of change in total bilirubin — mg/dl/hr‡		
Median	−0.07	0.00
Interquartile range	−0.20 to 0.02	−0.14 to 0.09
Efficacy — % (95% CI)	93 (89 to 96)	90 (86 to 93)
Safety		
Temperature checks — no.	1863	2160
Axillary temperature — °C‡		
Median	37.1	36.9
Interquartile range	36.7 to 37.5	36.6 to 37.2
Abnormal axillary temperature — no. (%)		
>39.0°C	1 (<1)	0
>38.0°C‡	85 (5)	15 (1)
<35.5°C‡	8 (<1)	2 (<1)
<35.0°C	0	0
Signs of dehydration — no. (%)	0	0
Signs of sunburn — no. (%)	0	0
Doctor called for any reason — no. (%)§	1 (<1)	0

* Efficacy is calculated as a percentage of treatment days that could be evaluated. Safety measures are expressed as a percentage of periodic temperature checks in infants. CI denotes confidence interval.

† Days that could be evaluated are defined as days on which the infant was able to tolerate at least 5 hours of phototherapy without meeting safety withdrawal criteria and on which both morning and afternoon bilirubin levels were measured.

‡ P<0.05.

§ The doctor was called by the study nurse for one infant who had peripheral cyanosis, which is normal in newborns.

burn.³⁶ However, many clinicians, even those in high-income countries, recommend the exposure of jaundiced babies to direct sunlight.³⁷ Some mothers, without the endorsement of health care workers, also continue to expose babies with jaundice to direct sunlight.^{36,38} In this trial, we used films that excluded virtually all ultraviolet light and some infrared light, maintained close surveillance, and used wet towels to avoid or treat hyperthermia.^{21,23} Our earlier survey of mothers showed that 98% would use filtered-sunlight phototherapy again and would recommend it to others.³⁹ Caregivers should therefore be educated on the essential differences between filtered sunlight and direct exposure to sunlight.

The current advantages of filtered sunlight include its availability in remote locations, the provision of treatment at the safest and most efficacious wavelength, and, when a large canopy is used, the increased opportunity for maternal–infant bonding, for the provision of skin-to-skin care, and for the feeding of infants when they are hungry. The energy source is free, and the cost of the film is low (\$0.55 and \$1.50 per square foot and \$44 and \$120 for a canopy for six to eight mother–infant pairs with Titanium and Air Blue 80 films, respectively, as compared with commercial phototherapy devices that cost between \$2,000 and \$3,500 per unit).^{21,40} However, open-air canopies require warm, sunny climates, which may not be available year-round in some low-to-middle-income countries,²³ and protection from storms and heavy rains. The provision of sunlight-based phototherapy in more durable, climate-controlled rooms rather than canopies would reduce the risks of hyperthermia and hypothermia but would also probably increase costs. Some infants treated with sunlight-based phototherapy (13% in our trial) also required nighttime phototherapy. Combining filtered sunlight with solar-powered phototherapy is one potential solution.

A limitation of the present trial is that we did not have infants with severe hyperbilirubinemia (bilirubin levels >15 mg per deciliter), who are at greater risk of acute bilirubin encephalopathy and are most likely to be admitted for treatment.^{10,24} Further studies are warranted to establish the efficacy of filtered-sunlight phototherapy among infants with severe hyperbilirubinemia who are not brought for treatment early in the course of disease.

In our post hoc exploratory analyses, higher levels of both bilirubin and of irradiance were associated with an increased rate of decline in bilirubin levels. These findings are consistent with those of previous studies of conventional phototherapy.^{33,34}

Existing guidelines for managing neonatal hyperbilirubinemia do not recommend — and some explicitly discourage — the use of sunlight for the treatment of neonatal hyperbilirubinemia.^{16,35} Reservations about the use of phototherapy with sunlight have reflected safety concerns regarding exposure to infrared and ultraviolet radiation, hyperthermia, and sun-

In conclusion, among infants with mild-to-moderate hyperbilirubinemia in tropical regions, the use of filtered-sunlight phototherapy resulted in manageable aberrations in temperature without serious adverse events. The treatment was no less efficacious than conventional phototherapy.

The preliminary findings of this study were presented at the Annual Pediatric Academic Societies Meeting, Vancouver, BC, Canada, May 3–6, 2014 (Late Breaker Session: Abstract No. 2823.7).

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The JM-103 transcutaneous bilirubinometer was loaned to the study by Draeger Medical; CPMs, a subsidiary of Eastman Chemical Company, donated the films; Advanced Instruments donated the Advanced BR2 Bilirubin Stat-Analyzer and provided the BR2 kits at a reduced cost; Dr. Lund donated the glucose-6-phosphate testing supplies; and Dr. Vreman donated most of the supplies for the canopy frames.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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