The effect of device position and use of transparent covers on the irradiance distribution of LED phototherapy devices

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Declaration

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Acknowledgements, format and contributions

This dissertation is submitted in the “already published” format according to the most recent UCT guidelines. The research has been published in the South African Journal of Child Health (SAJCH 2020;14(2):87-93). I wrote the protocol, collected the data, participated in data analysis and wrote the manuscript. Prof A Horn supervised all of the above and assisted with data analysis, interpretation of data and contributed to the writing and editing of the manuscript.

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It is my sincere wish that this research may be beneficial and contribute to the knowledge of appropriate use of LED phototherapy light

Abstract

Background

Effective phototherapy reduces neonatal jaundice and its complications. Irradiance increases as the distance of the light source decreases from a single phototherapy light. There are limited studies of the effect of distance and positional changes on different LED light designs on achieving effective phototherapy.

Objectives

To describe and compare the effect of distance, angle and plastic barriers on three different LED lights of different design.

Methods

Comparisons were made using a Servolite LED light, a General Electric (GE) Lullaby and a Ningbo David LED phototherapy light. Measurements were done according to methods described by the International Electrotechnical Communission (IEC). The effective irradiated area was measured on a grid measuring 60 x 30 cm subdivided into 5 x 5 cm squares. Measurements were done for the following scenarios: light placed at the manufacturers' recommended distance, 20 cm closer, 20 cm further, at an angle, through clear plastic and through scuffed perspex.

Results

When the lights were placed closer to the irradiated surface than the manufacturers' recommendations, the maximum irradiance increased, but the median irradiance and uniformity ratio decreased. When the lights were angled at 45° the median irradiance was decreased. A decrease in the median irradiance was also seen when phototherapy lights passed through scuffed plastic and food grade plastic.

Conclusion

Our study demonstrated that placing LED lights closer than the manufacturers recommendations, the use of transparent barriers and the use of lights at an angle, compromised phototherapy irradiance and distribution. Only the GE light met IEC standards.

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Abbreviations

AAP American Academy of Pediatrics

BIND Bilirubin induced neurologic dysfunction

BSA Body surface area

EIA Effective irradiated area

ESA Effective surface area

GE General electric

IEC International electrochemical communication

LED Light emitting diode

NNJ Neonatal jaundice

NICE National Institute for Healthcare and excellence guidelines

SA South African

Chapter 1

Abstract

Background

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Introduction

Neonatal jaundice (NNJ) occurs in the majority of healthy term and late-preterm newborns within the first week of life, owing to the accumulation of bilirubin in the blood.[1] Unconjugated bilirubin at high concentrations can cross the blood-brain barrier and cause bilirubin-induced neurological dysfunction (BIND), but effective phototherapy can prevent BIND.[2]

Phototherapy using light wavelengths corresponding to the absorption spectrum of bilirubin in the blue-green spectrum peaking at 460±30 nm, reduces serum bilirubin.[3,4] Intensive phototherapy was defined by the American Academy of Pediatrics (AAP) in 2004 as irradiance in the 430 - 490 nm spectrum, of at least 30 μW/cm^2/nm, 'measured at the infant's skin directly below the centre of the phototherapy unit'.[5] The South African (SA) phototherapy guidelines recommend the use of intensive phototherapy when total serum bilirubin (TSB) exceeds time-dependent thresholds.[6] If bilirubin levels continue to rise despite phototherapy, the AAP guidelines suggest bringing phototherapy lights closer to the infant to increase irradiance.[7] There are limited, device-specific studies showing a decrease in irradiance when a transparent barrier is placed between the neonate and the light source,[8-10] but neither the AAP nor the SA guidelines discuss the impact of transparent barriers. Despite the recommendations in the AAP guidelines, the manufacturers of light-emitting diode (LED) phototherapy devices in use at the authors' institution do not advocate using the device at a distance closer than the recommended distance; LED devices differ from older devices using fluorescent lights by having multiple small LED lights arranged with overlapping light cones. The device brochure for the General Electric (GE) Lullaby LED phototherapy light (GE Healthcare, Laurel, USA) states that the optical design ensures a uniform light distribution.[11] The focusing of the lights and strategic overlapping suggests that placement of LED devices closer to, or further away from, the infant will have a significant and probably negative effect on irradiance – different to the beneficial effect observed with fluorescent lights.

We hypothesised that placement of LED phototherapy devices closer than recommended by manufacturers will not achieve appropriate light intensity and distribution. We therefore aimed to compare the effect of phototherapy device position, distance and the presence of transparent barriers on the irradiance distribution maps of three devices frequently used in Cape Town, SA.

Objectives

1. To describe the irradiance distribution and the mean, maximum and minimum irradiance in the 420 - 480 nm spectrum in three LED phototherapy devices in the following situations:

    - at the distance recommended by the manufacturer with the device horizontally aligned and at 20 cm higher and 20 cm lower;

    - at the distance recommended by the manufacturer with a mildly scuffed incubator perspex hood between the device and the measuring radiometer;

    - at the distance recommended by the manufacturer with a single sheet of clear food-grade plastic bag between the device and the measuring radiometer;

    - at the distance recommended by the manufacturer with the device and aligned at an angle corresponding to the slope of an incubator.

2. To produce irradiance distribution maps for each of the devices and settings described above.

Methods

Study design and ethics approval

This was a bench-side observational study. The irradiance distributions of three phototherapy units were measured under different circumstances. The study was approved by the Paediatric Departmental Research Committee – approval from the Human Research Ethics Committee was not required because there were no human or animal participants.

The devices (the study sample)

Three new LED phototherapy devices were supplied by the distributors for comparison:

1. Servolite (SL) LED phototherapy light (Servocare Medical Industries, South Africa (SA), with five focused high-power blue LED lights producing overlapping light cones.

2. General Electric (GE) Lullaby LED phototherapy light (GE Healthcare, USA) with two separate clusters of high-power blue LED lights that produce two beams which overlap in the middle of the irradiated area.

3. Ningbo David (ND) XHZ-90L LED light (Ningbo David Medical Device Company,

China) with multiple blue LEDs spaced to create a broad beam of light.

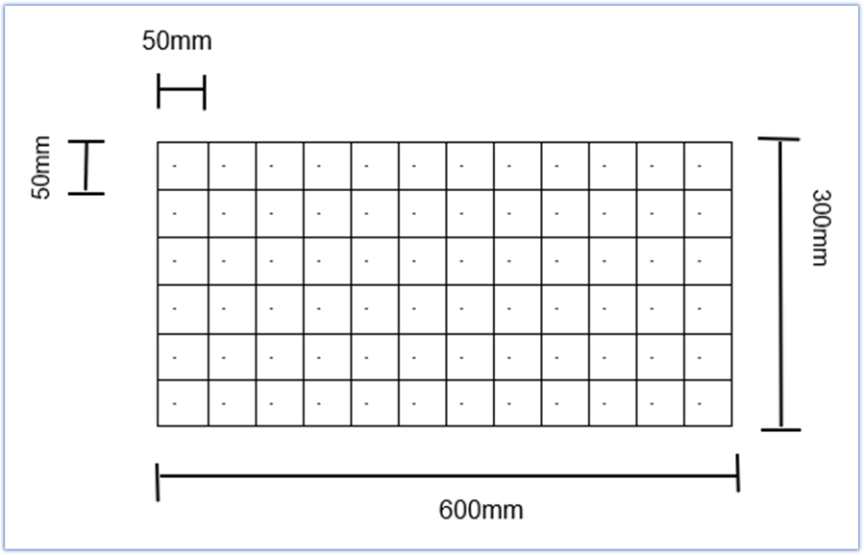
Data collection (irradiance measurement)

We used the standardised method of measuring irradiance distribution described by the International Electrotechnical Commission (IEC).[12] The IEC defines the effective irradiated area (EIA) as the 'intended treatment surface which is illuminated by phototherapy'. Previously, the EIA was referred to as the effective surface area (ESA). The IEC recommends an EIA of 60 cm × 30 cm with irradiance measurements on a grid with 10 cm or less separating each measurement. The EIA is further defined by the IEC as the area whereby the ratio of minimum irradiance to maximum irradiance, the uniformity ratio (UR), is > 40%. Irradiance should be measured with the phototherapy device at the height and position recommended by the manufacturer. Hence, the IEC recommends a desired value for minimum irradiance of 0.4 x maximum irradiance to ensure uniformity of irradiance.

We placed a 60 × 30 cm template, with a grid of 5 cm squares (Fig. 1) on the surface where irradiance was measured. Irradiance was measured using the Ohmeda Medical BiliBlanket Meter II (GE Healthcare, USA). This radiometer measures a spectral range of 400 - 520 nm with a centre wavelength of 450 nm and a bandwidth of 60 nm. The measuring range of its spectral irradiance is 0.1 - 2 99.9 $\mu W/cm^2/nm$. The manufacturer states that the device can be used to measure irradiance from LED, fluorescent, halogen and fibre-optic phototherapy devices. The Ohmeda radiometer was the preferred device for irradiance assessment by GE Healthcare – the manufacturers of the other two devices did not specify a preference in their brochures. Irradiance was measured by placing the radiometer in the centre of each square on the grid with the phototherapy device directed on it in different situations, as described below. The values obtained were recorded on a hard-copy grid and then entered into an Excel (Microsoft Corp., USA) spreadsheet with columns and rows labelled according to their position on the measuring grid.

Verman *et al*.[13] recommend measuring and plotting irradiance over a rectangular grid of 50 × 30 cm. They also recommend assessing irradiance over a silhouette of a term infant placed in the centre of the bed, with approximate length of 40 cm and approximate greatest width of 20 cm, to determine the percent treatable body surface area (BSA).[14]

Figure 1. The irradiance measuring grid.



Irradiance was measured for each device in the following scenarios:

1. The device was positioned above the middle of the grid, in the same position that it would be if the grid was enclosed in an incubator, horizontally orientated, using a spirit level, with no obstructions. Irradiance was measured at the height recommended by the manufacturer, at 20 cm higher (far position) and 20 cm lower (close position), measured with measuring tape and a plumb line from the centre of the device to the centre of the grid.

2. The device was positioned as above at the height recommended by the manufacturer with a single layer of food-grade clear plastic covering the light meter (but not touching it).

3. The device was positioned over a mildly scuffed incubator, the grid was placed on the mattress of the incubator, the light centred over the middle of the grid, horizontally orientated, at the height recommended by the manufacturer.

4. The device was positioned centrally but slightly to one side as it would be on the side of a closed incubator, orientated at an angle of 45 degrees, with no obstructions, at the height recommended by the manufacturer. The position as it would be with a closed incubator is shown in Fig. 2.

Figure 2: Angled position demonstrated with the GE device and a closed incubator

Data analysis

Stata Version 12 (StataCorp., USA) was used for statistical analysis. The mean, median, maximum and minimum irradiances and the UR were calculated for each scenario over the 60 × 30 cm grid and also when the EIA was decreased to 50 × 30 cm and 40 × 20 cm. Irradiance was represented graphically as a map or 'footprint' for each scenario. Since several data distributions within the light footprints were not symmetrical, median irradiance was compared using the Wilcoxon signed-rank test for matched samples.

Results

Measurements over an EIA defined by a 60 × 30 cm grid (1800 cm^2)

The irradiance measurements over the entire 60 × 30 cm grid for each device and setting are shown in Table 1 and Figs 3 - 5.

The frequent differences between mean and median irradiances demonstrate the non-normal distribution of the data. Minimum irradiance was below 2 $\mu W/cm^2/nm$ for all devices when positioned at the recommended distance. The UR was substantially less than 0.4 in all cases and it decreased further as lights were brought closer. When the devices were placed 20 cm closer than manufacturers' recommended distances (close position), the maximum and mean irradiance increased, and the median irradiance decreased compared with the mean irradiance, but the minimum irradiance decreased in all cases except the ND. The maximum irradiances at the close position were very high and ranged from 60 - 249.8 $\mu W/cm^2/nm$. All devices showed a very rapid fall-off in irradiance around the edges of a small high-intensity area when placed at the close position. When the GE was placed at the close position, this resulted in two separate small high-intensity patches of irradiance separated by very low irradiance between (Fig. 4).

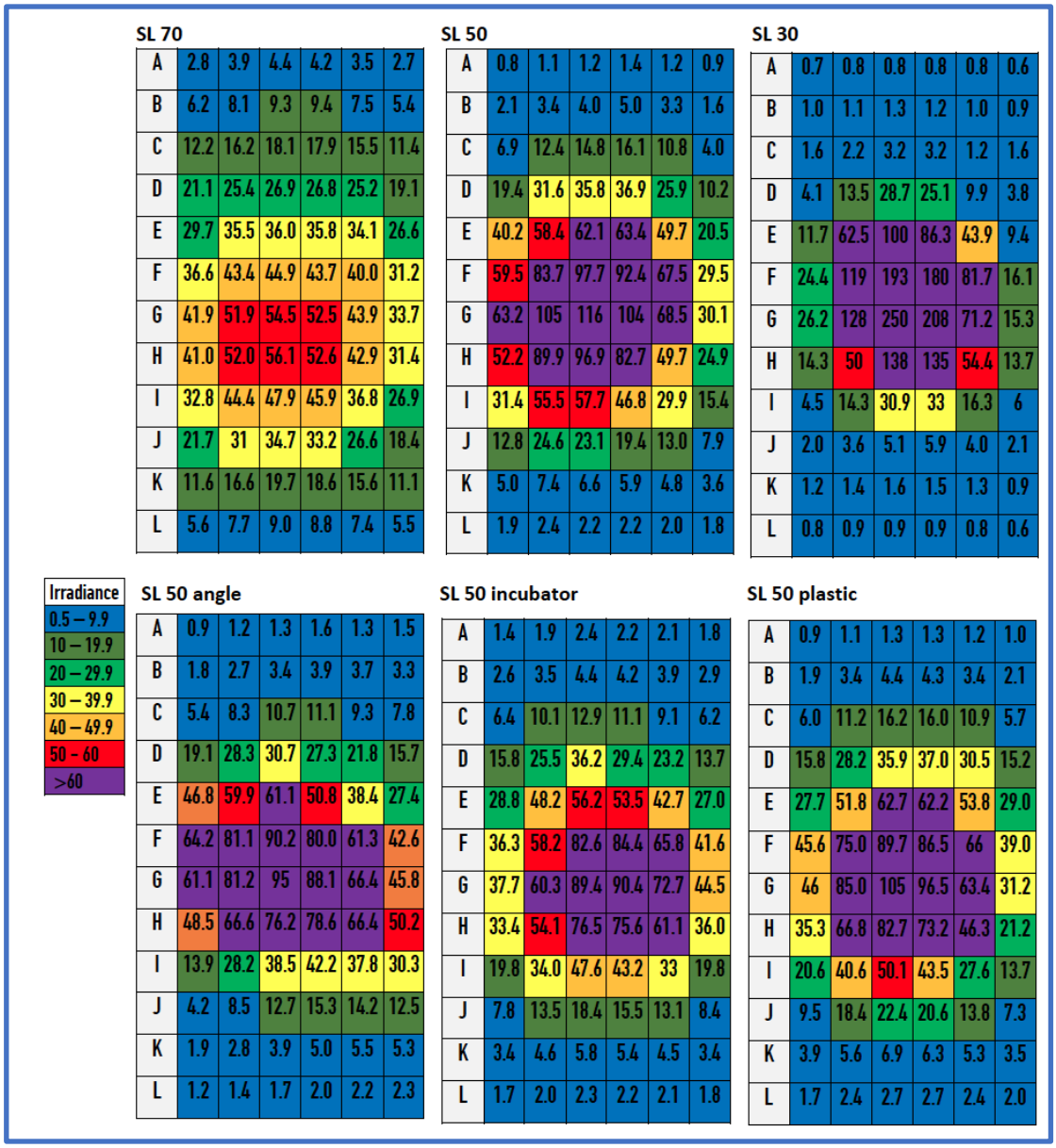
When the lights were angled at 45^o, the maximum irradiance decreased with the SL and GE, but increased with the ND. In this position, the median irradiance decreased by 27.8%, 7.6% and 13.9% in the SL, GE and ND, respectively. There was a marginal decrease in median irradiance when phototherapy light passed through mildly scuffed incubator plastic of 3.7%, 3.1% and 0.7% in the SL, GE and ND respectively – and maximum irradiance decreased in all devices. A single layer of food-grade plastic decreased the irradiances by 10.8%, 0.4% and 27.8% in the SL, GE and ND respectively – maximum irradiance decreased with the SL and ND but was marginally increased with the GE.

Table 1: Total irradiance for bilirubin using different phototherapy devices, distances and barriers on a 60 x 30 cm grid (1800 cm^2)

Device	Distance from surface (cm)	Barriers or angle	Max. irrad.*	Min. irrad.*	0.4 x Max. irrad.*‡	Min:Max Ratio (UR)	Mean irrad.* (SD)	Median irrad.* (IQR)	P value†
SL	70	None	56.1	2.7	22.4	0.048	25.4 (15.7)	26 (10.3–36.7)	0.535
SL	30	None	249.8	0.6	99.9	0.002	31.7 (55.4)	4.3 (1.2–29.8)	0.002
SL	50	None	115.8	0.8	13.8	0.007	31.1 (32.2)	19.4 (4–53.9)	§
SL	50	Angle	95	0.9	38	0.009	27.4 (28)	14 (3.6–47.7)	0.004
SL	50	Incubator	90.4	1.4	36.2	0.015	26 (25.8)	15.7 (1.4–90.4)	< 0.001
SL	50	Plastic	105.3	0.9	42.1	0.009	28.2 (28.4)	17.3 (4.1–45.8)	0.001
GE	55	None	33.1	9.2	13.2	0.278	19.6 (6.5)	19 (13.9–24.4)	< 0.001
GE	15	None	218.6	1.6	87.4	0.007	36.3 (51.4)	10.6 (5–56.5)	0.558
GE	35	None	60	2.5	24	0.042	28.6 (15.1)	27.5 (16.1–41.5)	§
GE	35	Angle	50.8	1.7	20.3	0.033	25.1 (13.3)	25.4 (15.4–36.4)	0.003
GE	35	Incubator	56.8	4.1	22.7	0.072	26.9 (13.6)	24.4 (16.6–38.3)	0.067
GE	35	Plastic	63.9	2.4	25.6	0.038	28.1 (15.1)	27.4 (15.4–41.7)	0.082
ND	70	None	34.4	1.9	13.8	0.055	15.3 (9.4)	14.7 (6.7–22.1)	0.011
ND	30	None	62.3	1.5	25	0.024	20.9 (19.9)	14.4 (3.2–40.4)	0.017
ND	50	None	49.5	1.3	19.8	0.026	17.6 (14)	15.1 (4.1–26.7)	§
ND	50	Angle	89.6	1.3	35.8	0.015	17 (14.9)	13 (4.6–26.4)	0.008
ND	50	Incubator	44.7	2	17.9	0.045	16.8 (12.6)	14.4 (5.4–25.5)	0.036
ND	50	Plastic	47	1.3	18.8	0.028	15.4 (13.5)	10.9 (4–25.1)	0.001

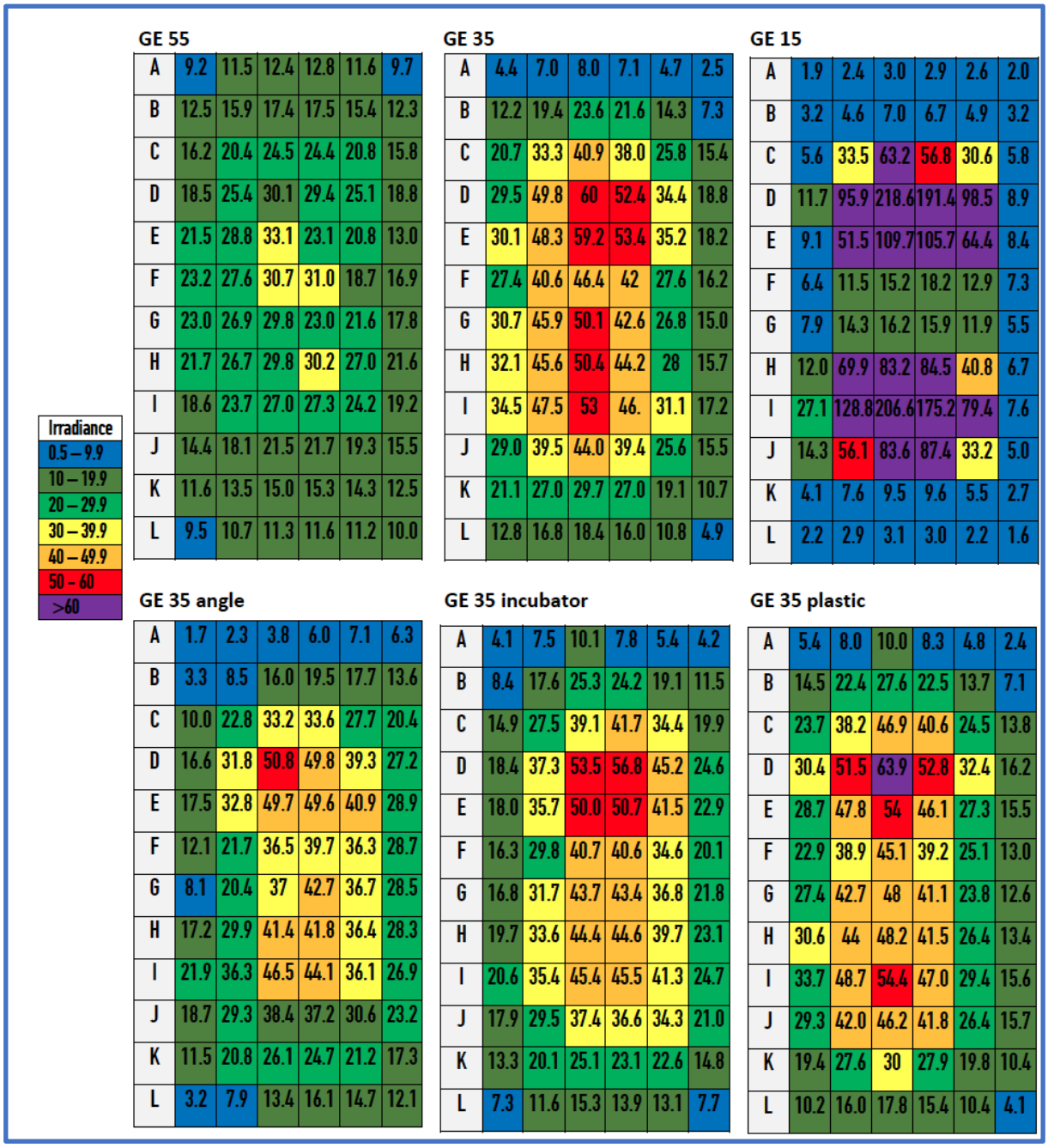
** µW/cm^2/nm; † p-value denotes comparison with standard recommended position and distance; ‡ 0.4 x Max. irrad is the desired value for minimum irradiance in order to comply with International Electrotechnical Commission uniformity recommendations; § no p-value as this is the recommended distance; GE – General Electric; irrad – irradiance; SD – Standard deviation; IQR – Interquartile range; SL – servolite; ND – Ningbo David*

Figure 3: The irradiance map of the Servolite (SL) phototherapy light in different settings



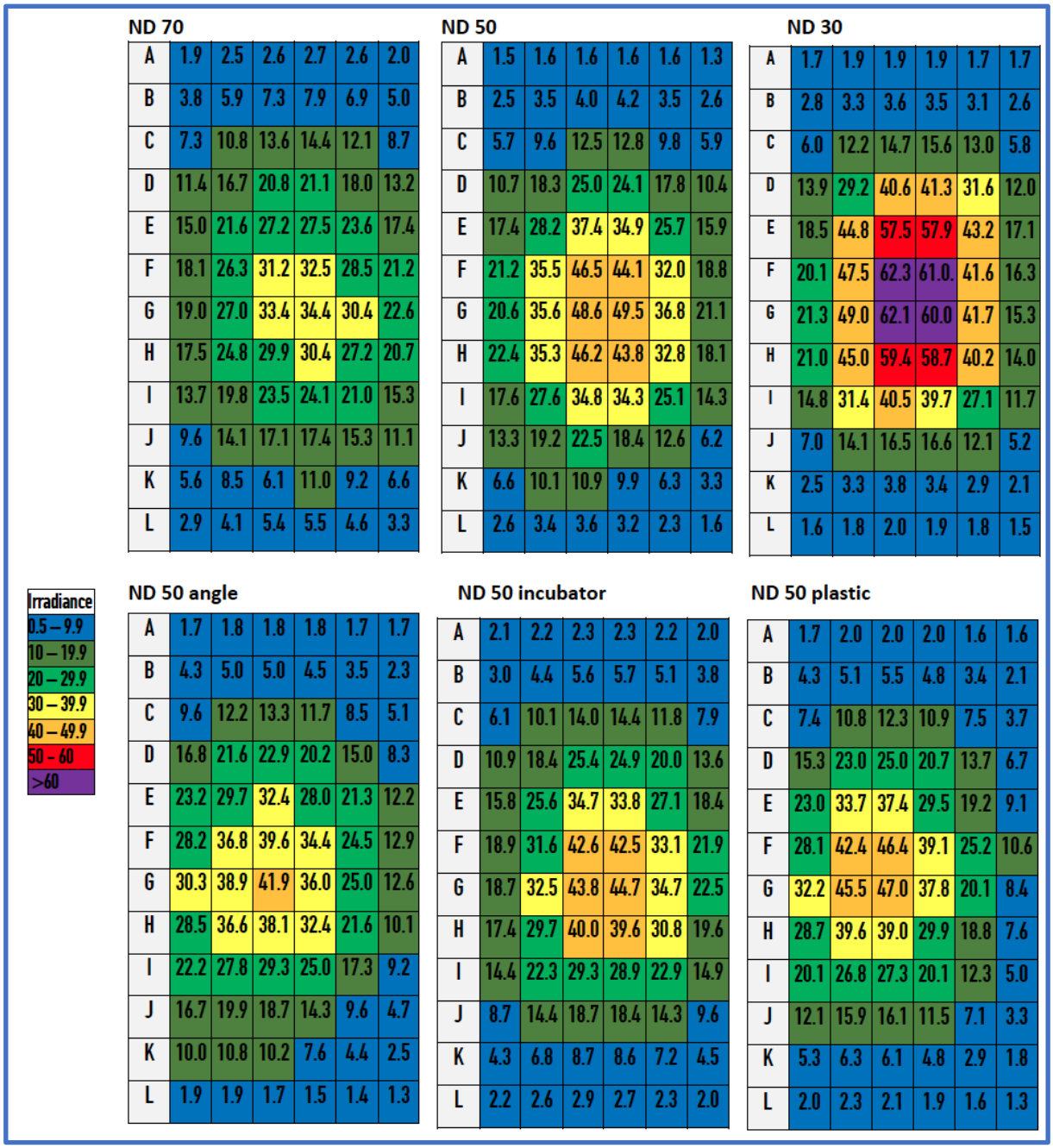
SL 70 – servolite at 70 cm; SL 50 – servolite at 50 cm; SL – 30 servolite at 30 cm; SL 50 angle – servolite at 50 cm at an angle; SL 50 incubator – Servolite at 50 cm through an incubator; SL 50 plastic – Servolite at 50 cm through food grade plastic

Figure 4: The irradiance map of the General Electric (GE) phototherapy light in different settings



GE 70 – General Electric at 70 cm; GE 50 – General Electric at 50 cm; GE 30 – General Electric at 30 cm; GE 50 angle – General Electric at 50 cm at an angle; GE 50 incubator – General Electric at 50 cm through an incubator; GE 50 plastic – General Electric at 50 cm through food grade plastic

Figure 5: The irradiance map of the Ningbo David (ND) phototherapy light in different settings



ND 70 – Ningbo David at 70 cm; ND 50 – Ningbo David at 50 cm; ND 30 – Ningbo David at 30 cm; ND 50 angle – Ningbo David at 50 cm at an angle; ND 50 incubator – Ningbo David at 50 cm through an incubator; ND 50 plastic – Ningbo David at 50 cm through food grade plastic

Measurements over an EIA of 50 x 30 cm (1500 cm^2)

The irradiance measurements when EIA is defined as 50 × 30 cm are shown in Table 2. The irradiance map for this area can be appreciated in Figs 3 - 5 by ignoring the first and the last rows. The maximum irradiance was the same as for the 60 × 30 cm grid, but minimum irradiance and UR only increased marginally. The only device with UR > 0.4 was the GE – at the far position. The UR for both the SC and the ND were highest at the far distance – and the minimum irradiance was highest at the far distance for these devices. The median irradiance was unchanged or decreased when transparent barriers were in place; the decrease ranged from 0 - 21%.

Measurements over an EIA of 40 x 20 cm (800 cm^2)

The irradiance measurements when EIA is defined as 40 × 20 cm are shown in Table 3. The pattern of variation in irradiance for these areas can be seen in Figs 3 - 5; the 40 × 20 cm area is obtained by ignoring the first two rows, the last two rows and the first and the last columns. The maximum irradiance was the same as for the 60 × 30 cm grid. The minimum irradiance and URs increased further compared with the 50 × 30 cm grid, but the GE was still the only device with UR > 0.4 – at all positions except the close position and when plastic covered the radiometer. The UR and the minimum irradiances for both the SC and the ND were again highest at the far distance. The changes in irradiance with devices angled at 45^0 were similar to those observed over the larger grids, but larger changes in irradiance were observed with transparent barriers in place. Decrease in irradiances through incubator plastic were: 18.2%, 7.2% and 7% for the SL, GE and ND, respectively. Decreases in irradiance through food- grade plastic were: 8.3%, 2.1% and 20.2% for the SL, GE and ND, respectively.

Table 2: Total irradiance for bilirubin using different phototherapy devices, distances and barriers on a 50 x 30 cm grid (1500 cm^2)

Device	Distance from surface (cm)	Barriers or angle	Max. irrad.*	Min. irrad.*	0.4 x max irrad.* ‡	Min:Max Ratio	Mean irrad.* (SD)	Median irrad.* (IQR)	P value †
SL	70	None	56.1	5.4	22.4	0.10	29.5 (14.1)	30.4 (18 – 41.5)	0.120
SL	30	None	249.8	0.9	99.9	< 0.01	37.9 (58.9)	10.8 (1.8–47)	0.021
SL	50	None	115.8	1.6	46.3	0.01	37 (32.2)	27.7 (9.1 – 59)	§
SL	50	Angle	95	1.8	38	0.02	32.5 (28)	27.4 (7.9– 55.4)	0.007
SL	50	Incubator	90.4	2.6	36.2	0.03	30.8 (25.7)	25.6 (8.1 – 46.1)	< 0.001
SL	50	Plastic	105.3	1.9	42.1	0.02	33.5 (28.2)	27.7 (8.4 – 51)	< 0.001
GE	55	None	33.1	11.6	13.2	0.40	21.3 (5.7)	21.5 (16.6 – 26.1)	< 0.001
GE	15	None	218.6	2.7	87.4	0.01	43 (53.9)	14.3 (7.2 – 67.2)	0.760
GE	35	None	60	7.3	24	0.10	32.4 (31.9)	30.4 (20.9 – 44.1)	§
GE	35	Angle	50.8	3.2	20.3	0.06	28.6 (11.7)	28.6 (20 – 36.9)	0.004
GE	35	Incubator	56.8	8.4	22.7	0.15	30.5 (11.9)	29.7 (20.1 – 40.7)	0.056
GE	35	Plastic	63.9	7.1	25.6	0.11	31.9 (13.6)	29.4 (22.5 – 43.4)	0.084
ND	70	None	34.4	3.8	13.8	0.11	17.7 (8.4)	17.4 (10.9 – 23.9)	< 0.001
ND	30	None	62.3	2.1	24.9	0.03	24.8 (19.7)	16.6 (6.5 – 41.5)	0.005
ND	50	None	49.5	2.5	19.8	0.05	20.7 (13.4)	18.4 (10 – 32.4)	§
ND	50	Angle	89.6	2.3	35.8	0.03	20.1 (14.5)	18 (9.8 – 28.4)	0.013
ND	50	Incubator	44.7	3	17.9	0.07	19.7 (11.8)	18.4 (9.2 – 29.1)	0.009
ND	50	Plastic	47	1.8	18.8	0.04	18.1 (13.2)	14.5 (6.5 – 27.7)	0.002

** µW/cm^2/nm; † p-value denotes comparison with standard recommended position and distance; ‡ 0.4 x Max. irrad. is the desired value for minimum irradiance in order to comply with International Electrotechnical Commission uniformity recommendations; § no p-value as this is the recommended distance; GE – General Electric; irrad – irradiance; IQR – Interquartile range; SD – Standard deviation; SL – servolite; ND – Ningbo David*

Table 3: Total irradiance for bilirubin using different phototherapy devices, distances and barriers on a 40 x 20 cm grid (800 cm^2)

Device	Distance from surface (cm)	Barriers or angle	Max. irrad.*	Min. irrad.*	0.4 x max irrad.* ‡	Min:Max Ratio	Mean irrad.* (SD)	Median irrad.* (IQR)	P value †
SL	70	None	56.1	15.5	22.4	0.28	37.3 (11.9)	36.4 (26.9 – 45.4)	< 0.001
SL	30	None	249.8	1.2	99.9	< 0.01	65.6 (69.6)	38.5 (7.9 – 110)	0.694
SL	50	None	115.8	10.8	46.3	0.10	54.4 (31.9)	52.6 (25.3 – 83.2)	§
SL	50	Angle	95	8	38	0.08	44.2 (28.7)	38.5 (14.8 – 66.5)	< 0.001
SL	50	Incubator	90.4	9.1	36.2	0.1	44.3 (26)	43 (20.9 – 63.5)	< 0.001
SL	50	Plastic	105.3	10.9	42.1	0.1	49.7 (27.7)	48.2 (25 – 70)	< 0.001
GE	55	None	33.1	18.1	13.2	0.55	25.4 (4.1)	25.2 (21.7 – 29.1)	< 0.001
GE	15	None	218.6	11.5	87.4	0.05	73.9 (58.3)	63.8 (24.4 – 97.2)	0.003
GE	35	None	60	25.6	24	0.43	42.1 (9.5)	43.3 (34.8 – 49.1)	§
GE	35	Angle	50.8	20.4	20.3	0.4	36.9 (7.9)	36.6 (32.2 – 41.6)	0.004
GE	35	Incubator	56.8	27.5	22.7	0.48	40.1 (6.9)	40.2 (35 – 44.5)	0.161
GE	35	Plastic	63.9	23.8	25.6	0.37	41.3 (10.1)	42.4 (35.3 – 47.9)	0.221
ND	70	None	34.4	10.8	13.8	0.31	23 (6.7)	23.6 (17.3 – 28)	< 0.001
ND	30	None	62.3	12.1	24.9	0.19	38.4 (17.1)	41 (21.9 – 53.3)	< 0.001
ND	50	None	49.5	9.6	19.8	0.19	29.2 (11.8)	30.1 (18.8 – 36.2)	§
ND	50	Angle	89.6	8.5	35.8	0.09	25.1 (9.7)	24.8 (18 – 33.4)	< 0.001
ND	50	Incubator	44.7	10.1	17.9	0.23	27.3 (10.1)	28 (18.6 – 34.2)	0.001
ND	50	Plastic	47	7.1	18.8	0.15	25.4 (12.3)	24 (14.8 – 37.6)	0.002

** µW/cm^2/nm; † p-value denotes comparison with standard recommended position and distance; ‡ 0.4 x Max. irrad. is the desired value for minimum irradiance in order to comply with International Electrotechnical Commission uniformity recommendations; § no p-value as this is the recommended distance; GE – General Electric; irrad – irradiance; IQR – Interquartile range; SD – Standard deviation SL – servolite; ND – Ningbo David*

Discussion

Three different LED phototherapy lights were chosen for the study based on their frequency of use and their design. The designs included overlapping beams from clustered LEDs, focused beams from overlapping light cones, and multiple LED's spaced out to create a broad beam of light.

The present study demonstrates that the distribution of irradiance intensity changes substantially when placing these LED phototherapy devices 20 cm closer or further away from the target treatment surface. Placing the devices 20 cm closer than recommended by manufacturers resulted in a large increase in maximum irradiance, but minimum irradiance was decreased to levels well below 8–10 μW/cm^2/nm in peripheral areas and, in the case of the GE device, also in the central area of the light footprint – these decreases resulted in a substantial reduction of the effective irradiated area. Irradiance intensity changed by over 100 μW/cm^2/nm within as little as 5 cm in several cases but there was wide variation between the devices. The placement of incubator or food-grade plastic between the device and the therapeutic target had marginal effect on maximum irradiance but decreased median irradiance in all devices over 40 x 20 cm grid, by up to 20%. There were similar changes when using the device at an angle, but the maximum irradiance increased by over 80% with the ND.

The IEC do not stipulate a minimum or maximum irradiance, since the optimal irradiance of phototherapy has not yet been established.[12] An irradiance of 8–10 μW/cm^2/nm was defined by the AAP in 1994 as "standard phototherapy" – this was based on the irradiance of "conventional" or "standard daylight units" at a distance of 20 cm. [15] The AAP recommend standard phototherapy when bilirubin levels are 34–51 μmol/l below the threshold for intensive phototherapy'.[1, 15] The AAP 2004 guidelines suggest that optimal irradiance is 30 μW/cm^2/nm, also referred to as 'intensive phototherapy' - based on data at the time suggesting that higher intensities would not be effective at lowering bilirubin levels.[5] However, previous and more recent studies using LED phototherapy lights have shown a linear correlation between light irradiance at 5–55 μW/cm^2/nm and percentage change in serum bilirubin – the linear relationship suggests that saturation will not occur at higher doses. [3] [4]

Hence doses of 30–55 μW/cm^2/nm may be considered optimal, spread evenly over the surface area of the neonate with UR of > 0.4.

The practice of bringing phototherapy lights closer was recommended at the time when special blue fluorescent bulbs were commonly in use.[5] Light intensity with these lights is inversely related to the distance from the source and, when these lights are moved closer to infants, the serum bilirubin level falls more rapidly. [16] The National Institute for Health Care and Excellence (NICE) guidelines, developed in the United Kingdom and updated in 2016, do not refer to 'optimal' or 'intensive' phototherapy – they refer only to 'phototherapy' and 'intensified phototherapy' without defining these terms with irradiance measures. [17] They suggest 'increasing the irradiance of the original light source' or adding more lights and they state that phototherapy devices should be used according to manufacturers' instructions.

Although a randomized trial of aggressive versus conservative phototherapy in preterm infants showed improved neurodevelopmental outcomes with aggressive phototherapy and no significant effect on death [18], there are concerns that prolonged phototherapy may be associated with DNA damage; the occurrence of very high irradiances focused on small areas when placing the devices close may not be safe. [19] A preferable approach may be to select a higher-intensity setting (if the device offers it). Alternatively, additional lights could be added so that the lights remain focused in the optimal position, increased surface area of skin is exposed, and there is a more uniform increase in irradiance. This is a topic for further study.

The large variation in irradiance intensities when phototherapy devices are moved very close to the therapeutic target which is further demonstrated by very low UR. The UR of > 0.4 required by IEC precludes the use of any devices we studied in the close position.[12] When used at recommended distances, only the GE device achieved this ratio in our study, and only over an EIA of 40 x 20 cm.

UR decreases with decreasing size of the EIA. Treatment of babies smaller than this size is expected to be associated with improved UR and higher minimum irradiance. The ND and SL (at 50 and 70 cm, respectively) may provide irradiance at levels in line with IEC

recommendations when applied to the small area of a preterm baby – this concept should be explored in further research.

Several methods of assessing irradiance, other than those of the IEC and Vreman *et al*, have been recommended.[20-22] Dicken *et al*.[20] measured irradiance levels over a rectangular area, based on the assumption that one-third of skin surface area is available for treatment – irradiance was measured over 20 cm × 35 cm for term neonates. Subramanian *et al*.[21] recommended measuring irradiance at 5 cm intervals over a rectangular grid of 60 cm × 30 cm and then tracing onto the grid an outline of a term baby with a two-dimensional surface area of 780 cm^2 to determine the BSA. Irradiance was measured at the centre and at four peripheral points and maximum, minimum and mean irradiance were measured within the outline of the neonate.

Reda *et al*.[22] recommended measuring and plotting irradiance at 7.5 cm intervals over a rectangular grid of 60 cm × 30 cm. We did not use an infant silhouette and we did not calculate treatable BSA, because the measurement of treatable BSA assumes that the infant lies still throughout treatment and that light approaches in a single plane, which is not the case. This method is also complex and the actual size of the silhouette and minimum irradiance to define 'treatment' have not been clearly defined, making it a difficult method to reproduce. Instead, we measured irradiance parameters over a 40 × 20 cm area, which is similar to the rectangular space occupied by a baby, is the area that lights are focused around in practice, and is also similar to the area described by Dicken *et al*.[20]

In addition to irradiance variation with height, the presence of physical barriers to light around neonates can also have an effect. Phototherapy irradiance provided with fluorescent bulbs decreases with the use of plastic blankets and heat shields. [8,9] A decrease in irradiance has also been described when phototherapy is applied through a scratched incubator surface.[10] Our data with LED lights are similar.

The present study has several limitations. Each irradiance measurement was only taken once. However, 72 measurements were taken on each grid and the consistency of measurements can be appreciated from the irradiance maps (Figs 3 - 5). The operation and maintenance manual

states that the Ohmeda Medical BiliBlanket Meter II measures irradiance continually with an accuracy of ~3%. We performed a *post hoc* evaluation of accuracy by taking 72 measurements (the number of measurements in each grid) in the same position. The mean (standard deviation) of 72 measurements taken at 35 cm below the centre of the Lullaby device was 39.6 (0.1) $\mu W/cm^2/nm$. Further limitations are: only one device of each type was evaluated; and the distance between the plastic cover and the light source may have had a more profound effect than we observed without the cover. The positions used were based on what is done in clinical practice.

Conclusion

We have demonstrated that the most appropriate distance to place LED phototherapy lights depends on the design of the lights. Placing lights closer than recommended significantly compromises the light distribution and irradiance. The use of transparent barriers decreases irradiance further. All three lights had maximum irradiance of at least 30 $uW/cm^2/nm$ (sufficient for intensive phototherapy) at all the distances, but minimum irradiance was only ≥ 8 $uW/cm^2/nm$ (sufficient for standard phototherapy) for most devices over the small grid of 40 × 20 cm. The UR only met IEC-recommended standards with the GE light. The SL device had improved uniformity with acceptable irradiance when used at 70 cm rather than the recommended 50 cm.

Although the GE device is the only device that meets both IEC and AAP recommendations for standard and intensive phototherapy, it only does so over a 40 × 20 cm grid. There is no evidence to show that the use of device with uniformity ratios < 0.4, very high maximum irradiance and low minimum irradiances below 8 $uW/cm^2/nm$ is associated with unacceptable performance.

Clinicians should be aware of the recommended distance and the shortcomings of phototherapy devices. Further research is needed to (*i*) evaluate consistency of performance between devices from the same manufacturer; (*ii*) determine the effect that distance and angle have on irradiance when barriers are used; (*iii*) determine the effect on irradiance of using more than one light; and (*iv*) determine simple rapid bedside irradiance assessment methods. The terms ‘intensive’

and ‘standard’ are misleading and poorly defined – there is a need to establish more appropriate terms that adequately describe the dose of phototherapy being given.

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Appendix 1: SAJCH reviewers' comments and author responses

Reviewer 1

This study involved measuring the irradiance of three different LED phototherapy lights available in the authors' neonatal unit in South Africa - no human subjects were involved. The methods are clearly described and the results clearly presented. The discussion is scientifically sound but concentrates on the technical aspects of the study.

The readership of the SAJCH is largely clinicians working in the field of paediatrics and in my view would find this paper too technical. While they do make some recommendations regarding using the various lights according to the manufacturer's specification with regard to the distance from the subject, there is very little else in the way of take- home messages for clinicians. While the information may be derived from the data presented, it would be useful in the discussion if they made more recommendations for clinicians e.g.

1.1 Are all three lights acceptable for standard phototherapy?

Author reply: All three lights had maximum irradiance of at least 30 uW/cm²/nm (intensive phototherapy) at all the distances and over all the grid sizes. The maximum irradiance of the SL was exceptionally high at the recommended distance but when used at 20 cm further away (at 70cm) was similar to the GE with improved UR. Minimum irradiance was only consistently above 8 uW/cm²/nm (standard phototherapy) over the small grid of 40 x 20cm. The only light that met IEC recommended standards with UR ≥ 0.4, was the GE light over an area of 40 x 30 cm or less.

The GE device is therefore the only device that meets both IEC and AAP recommendations for standard and intensive phototherapy. there is no evidence to show that the uniformity ratios of < 0.4 and minimum irradiances below 8 uW/cm²/nm are associated with unacceptable performance. The SL device performs closest to IEC recommendations when used at 70 cm distance rather than the recommended 50cm.

The conclusion has been amended to reflect the above.

1.2 Are all three lights acceptable for "intensive" phototherapy or would one of these be preferred?

Author reply: See above.

1.3 Since the mean length for premature babies <31 weeks gestation is <40cm, do their data for the 40 X 20 cm map suggest any different recommendations for these very premature babies?

Author reply: The UR decreases with decreasing size of grid. Treatment of babies smaller than this size is expected to be associated with improved UR and higher minimum irradiance. The ND and SL (at 50 and 70cm respectively may provide irradiance at levels in line with IEC recommendations when applied to the smaller area of a preterm baby – this concept should be explored in further research. The discussion and conclusion have been amended to reflect this.

Reviewer 2

Introduction

2.1

It may be relevant (either here or in the discussion) to raise the issue of differences between older phototherapy devices (using fluorescent light sources) and the more modern units using LED light sources. (I suspect that one of the important features of the LED systems is that the bulbs are sited within a frame that ensures that beams are focused on the areas of interest. If there is indeed focusing of the beams by the shape of the unit, then the exact distance from the surface would be expected to make a substantial difference. My understanding is that in general the intensity of light decreases by the square of the distance from the source.

However, if light is coming in beams that are being focused on particular areas, then this relationship will be different.) Provide a rationale for the importance of using recommended distances between light source and patient.

Author response: Thank you. A paragraph summarising the statement below has been added to the introduction, and clearer description of the layout and light orientation of each devise has been added to the methods section.

LED devices differ from older devices using fluorescent light in the way that multiple small lights are arranged with overlapping light cones. The GE device brochure states that the optical design ensures a uniform light distribution. The focusing of the lights and likely strategic overlapping suggests that placement of LED devices closer or further away from the infant will have a significant effect on irradiance and the effect can be expected to that observed with fluorescent lights.

Methods

2.2

It seems that measurements were done once only in each position, and with only one device from each manufacturer. It may be important to evaluate the reproducibility of the measurements, and also to evaluate the difference between devices (from the same manufacturer).

Author response: This aspect has been discussed further in the discussion and stated as a limitation.

Although each measurement was only taken once, 72 measurements were taken on each grid and the consistency of measurement can be appreciated from the irradiance map. The operation and maintenance manual states that the Ohmeda Medical BiliBlanket® Meter II measures irradiance continually with an accuracy of ± 3%. The variation in individual measurements has subsequently been further demonstrated by taking 72 measurements (the number of measurements in each grid) in the same position to show the standard deviation of the measurement method. The mean (standard deviation) of 72 measurements taken at 35cm below the centre of the lullaby device was 39.6 (0.1) $\mu W/cm^2/nm^2$.

The potential variation between devices from the same manufacturer is relevant but was beyond the scope of this study – the lack of this data has been stated as both a limitation and a further area of research.

2.3

I am interested at the distance between the light source and the "cover" (either the scuffed incubator cover or the sheet of plastic). Is it possible that the distance between the "cover" and the light source makes a difference? It would also be very interesting to know whether the angle of the "cover" makes a difference - it seems likely that if light strikes the "cover" at an angle there is likely to be more reflection of light from the "cover", and this has the possibility to make a substantial difference to the light intensity reaching the measuring surface. This may be relevant in the practical situation as some phototherapy units are angled deliberately (to avoid having the light source directly under the open incubator heat source).

Author response: It is possible that the distance between the cover and the light source makes a difference. The positions used were based on what is done in clinical practice. The testing and reporting of this hypothesis is beyond the scope of the current study – noting the word limit. However, this has been added as an area for further study in the discussion and conclusion.

2.3

I don't really understand why the device was kept centred over the measurement panel when it was angled. Surely it would have made more sense to move the device to one side so that the central point of the light intensity remained on the centre of the grid (alternatively that could be utilized as an additional position).

Author response: The device was infact moved to one side as described by the reviewer, but was aligned in a central position as it would be on the side of a closed incubator. This has been clarified in the methods and a figure has been added to demonstrate the position with a closed incubator for reference.

Results

Tables

2.4 The authors have not made it clear what comparison is reflected by the p-value.

Author response: The p-value denotes the comparison with the standard recommended position and distance. The footnotes of the Tables have been amended accordingly.

2.5 It is difficult to understand the reason for including a column of "0.4 x Max. irrad". It would be useful to have an explanatory text for the table.

Author response: The data collection section under methods states. "The EIA is further defined by the IEC as the area whereby the ratio of minimum irradiance to maximum irradiance, the uniformity ratio (UR), is > 40 %". An explanatory foot note has been added to the tables and the statement in the data section has been clarified.

2.6 I am assuming that the mean has standard deviation in brackets, and the median range in brackets. It would be better to make this clear in the tables

Author response: These abbreviations have been added to the tables and the footnotes.

Figures

2.7

The figures are interesting, showing that the shape of the maximum light intensity varies by manufacturer. It does seem as if the devices are constructed to focus light intensity on specific areas of distribution, and I would appreciate it if the authors could address the question of how the different manufacturers have chosen to focus the beams from their particular devices.

Author response: This has been dealt with in 2.1

Discussion

2.8

Is the effectiveness of phototherapy the same on all areas of the body (are the areas where phototherapy is more effective? E.g. if the baby has hair would phototherapy on the head be less effective?).

Author response: Phototherapy is most effective on areas with the highest surface area which implies no obstructions such as hair or clothing (Maisels 1996). This has not been added to the discussion due to word count limitations.

2.9

Does a decrease in phototherapy intensity on one area of the body get offset by an increase in light intensity on another area.

Author response: A decrease in phototherapy intensity on one area of the body could be offset by an increase in another area if the surface area of the two regions is the same. This has been left out of the discussion due to word count limitations.

2.10

My sense from the figures and the results is that the phenomenon being described could possibly be explained by the devices being manufactured to focus light on particular areas (from the reflective services behind the LEDs, and from the overall shape of the device). That is a significant difference from the older fluorescent bulbs which were simply arranged in a linear pattern in many units).

*Author response: Discussed in **2.1***

Conclusion

2.11

I am not sure why the authors have inserted the comment that it may be more effective to add additional lights. They have not examined that question, nor have they produced any data on that issue.

Author response. The addition of additional lights is expected to expose a larger surface area due to the different angles of the lights while increasing the minimal irradiance due to overlap. This could be an area for further research. The reference to it has been moderated by adding the word, "may" and providing further explanation in the discussion.

Appendix 2: Research approval from DRC

SCAH# 10/8/18

Form D1(a) – for MMed and MPhil (sub-specialty) registrars to submit with study proposal

University of Cape Town, Faculty of Health Sciences

Form D1(a): Scientific and educational validity form for specialty/subspecialty MMed/MPhil degrees

(from2013)

Study Title: The effect of device position and use of transparent covers on the irradiance distribution of LED phototherapy devices

The Synopsis is complete and presented according to UCT HREC guidelines, form FHS014.	Yes / No

Where minor changes are needed, indicate on the protocol; where major changes are needed, please attach comments on a separate page

PROTOCOL	No change	Minor change	Major change
1. The purpose and background (literature review) are appropriately presented. The setting, current practice and gaps in the literature are described to provide sufficient rationale to justify the purpose of the study and to contextualise the importance/relevance of the study.	✓		
2. The objectives are clearly stated, linked to the purpose and are feasible within the available time and resources	✓		
3. Methodology: a. The design is appropriate to the objectives, is feasible and is adequately funded b. The method is written in sufficient detail for publication purposes c. The sample characteristics and size are described and justified in the context of the objectives; and the recruitment/sampling method is appropriate Studies that aim to compare one treatment/intervention/scenario with another as a primary objective have power calculations provided unless they are primarily exploratory and/or establishing baseline data for the context d. There is a clear description of which data will be collected, by whom and how it relates to the objectives e. The data reporting and statistical analysis methods are appropriately described (including: electronic programme e.g. Excel, Stata, other; appropriate tests; and probability levels/confidence boundaries (if applicable) f. The limitations of the methodology are discussed	✓		
4. The ethical considerations are clearly and appropriately described. Research subjects assured of confidentiality, anonymity and respect. Data storage is appropriate. Possible adverse effects or risks associated with the audit outcomes described. Consent procedure is described (or lack of consent justified) and associated forms are attached. The data dissemination procedures at the end of the study and subsequent patient/situational management are described. The process of obtaining institutional, ethical and provincial approval is described.	✓		
5. All references are included with the same referencing format throughout.	✓		
6. The literary style of writing and presentation is acceptable.	✓		
7. The proposal is scientifically suitable for an MMed / MPhil in keeping with the current UCT guidelines.	✓		
8. Appropriate appendices are attached. (including consent and assent form (if appropriate); budget; and data collection forms)	✓		

My signature below confirms that the protocol named above meets the requirements for [illegible] minor dissertation, submitted by: Dr Muganmad Talb Ismail (Registrar Name)

Signed: ..... Name .....

Professor Brenda Morrow
Chair
2018 -11- 19
Department of Paediatrics & Child Health

Capacity: (ring) Departmental Research Chair/Registrar review committee chair/delegate/representative

Appendix 3: SAJCH Journal instructions to authors

Manuscript preparation

Preparing an article for anonymous review

To ensure a fair and unbiased review process, all submissions are to include an anonymised version of the manuscript. The exceptions to this requirement are Editorials, Correspondence, Book reviews and Obituary submissions.

Submitting a manuscript that needs additional blinding can slow down your review process, so please be sure to follow these simple guidelines as much as possible:

- An anonymous version should not contain any author, affiliation or particular institutional details that will enable identification.
- Please remove title page, acknowledgements, contact details, funding grants to a named person, and any running headers of author names.
- Mask self-citations by referring to your own work in third person.

General article format/layout

Submitted manuscripts that are not in the correct format specified in these guidelines will be returned to the author(s) for correction prior to being sent for review, which will delay publication.

General:

- Manuscripts must be written in UK English (this includes spelling).
- The manuscript must be in Microsoft Word or RTF document format. Text must be 1.5 line spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes). Pages and lines should be numbered consecutively.
- Please make your article concise, even if it is below the word limit.
- Qualifications, ***full*** affiliation (department, school/faculty, institution, city, country) and contact details of ALL authors must be provided in the manuscript and in the online submission process.
- Abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.
- Scientific measurements must be expressed in SI units except: blood pressure (mmHg) and haemoglobin (g/dL).
- Litres is denoted with an uppercase L e.g. 'mL' for millilitres).
- Units should be preceded by a space (except for % and ºC), e.g. '40 kg' and '20 cm' but '50%' and '19ºC'.
- Please be sure to insert proper symbols e.g. µ not u for micro, a not a for alpha, b not B for beta, etc.
- Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160.
- Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'
- Round brackets (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.

If you wish material to be in a box, simply indicate this in the text. You may use the table format –this is the *only* exception. Please DO NOT use fill, format lines and so on.

SAJCH is a Journal on child health, therefore for articles involving genetics, it is the responsibility of authors to apply the following:

- Please ensure that all genes are in italics, and proteins/enzymes/hormones are not.
- Ensure that all genes are presented in the correct case e.g. TP53 not Tp53.

** NB: Copyeditors cannot be expected to pick up and correct errors wrt the above, although they will raise queries where concerned.

- Define all genes, proteins and related shorthand terms at first mention, e.g. '188del11' can be glossed as 'an 11 bp deletion at nucleotide 188.'
- Use the latest approved gene or protein symbol as appropriate:

- Human Gene Mapping Workshop (HGMW): genetic notations and symbols
- HUGO Gene Nomenclature Committee: approved gene symbols and nomenclature
- OMIM: Online Mendelian Inheritance in Man (MIM) nomenclature and instructions
- Bennet et al. Standardized human pedigree nomenclature: Update and assessment of the recommendations of the National Society of Genetic Counselors. J Genet Counsel 2008;17:424-433: standard human pedigree nomenclature.

Preparation notes by article type

Research

Guideline word limit: 3 000 words (excluding abstract and bibliography)

Research articles describe the background, methods, results and conclusions of an original research study. The article should contain the following sections: introduction, methods, results, discussion and conclusion, and should include a structured abstract (see below). The introduction should be concise – no more than three paragraphs – on the background to the research question, and must include references to other relevant published studies that clearly lay out the rationale for conducting the study. Some common reasons for conducting a study are: to fill a gap in the literature, a logical extension of previous work, or to answer an important clinical question. If other papers related to the same study have been published previously, please make sure to refer to them specifically. Describe the study methods in as much detail as possible so that others would be able to replicate the study should they need to. Where appropriate, sample size calculations should be included to demonstrate that the study is not underpowered. Results should describe the study sample as well as the findings from the study itself, but all interpretation of findings must be kept in the discussion section, which should consider primary outcomes first before any secondary or tertiary findings or post-hoc analyses. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

- May include up to 6 illustrations or tables.
- A max of 20 - 25references

Structured abstract

- This should be no more than 250words, with the following recommended headings:
  - **Background:** why the study is being done and how it relates to other published work.
  - **Objectives:** what the study intends to find out
  - **Methods:** must include study design, number of participants, description of the intervention, primary and secondary outcomes, any specific analyses that were done on the data.
  - **Results:** first sentence must be brief population and sample description; outline the results according to the methods described. Primary outcomes must be described first, even if they are not the most significant findings of the study.

- **Conclusion:** must be supported by the data, include recommendations for further study/actions.
- Please ensure that the structured abstract is complete, accurate and clear and has been approved by all authors. It should be able to be intelligible to the reader without referral to the main body of the article.
- Do not include any references in the abstracts.

Here is an example of a good abstract.

***Scientific letters*/short reports**

These include case reports, side effects of drugs and brief or negative research findings.

Guideline word limit: 1500 words

- Abstract: unstructured, of about 100-150 words
- May include only one illustration or table
- A maximum of 6 references

Editorials

Guideline word limit: 1 000 words

These opinion or comment articles are usually commissioned but we are happy to consider and peer review unsolicited editorials. Editorials should be accessible and interesting to readers without specialist knowledge of the subject under discussion and should have an element of topicality (why is a comment on this issue relevant now?) There should be a clear message to the piece, supported by evidence.

Please make clear the type of evidence that supports each key statement, e.g.:

- expert opinion
- personal clinical experience
- observational studies
- trials
- systematic reviews.

Review articles

Review articlesshould always be discussed with the Editor prior to submission.

Guideline word limit: 4 000 words

These are welcome, but should be either commissioned or discussed with the Editor before submission. A review article should provide a clear, up-to-date account of the topic and be aimed at non-specialist hospital doctors and general practitioners. They should be aligned to practice in South and/or sub-Saharan Africa and not a precis of reviews published in the international literature

Please ensure that your article includes:

- Abstract: unstructured, of about 100-150 words, explaining the review and why it is important

- Methods: Outline the sources and selection methods, including search strategy and keywords used for identifying references from online bibliographic databases. Discuss the quality of evidence.
- When writing: clarify the evidence you used for key statements and the strength of the evidence. Do not present statements or opinions without such evidence, or if you have to, say that there is little or no evidence and that this is opinion. Avoid specialist jargon and abbreviations, and provide advice specific to southern Africa.
- Personal details: Please supply your qualifications, position and affiliations and MP number (used for CPD points); address, telephone number and fax number, and your e-mail address; and a short personal profile (50 words) and a few words about your current fields of interest.

Correspondence (Letters to the Editor)

Guideline word limit: 400 words

Letters to the editor should relate either to a paper or article published by the SAJCH or to a topical issue of particular relevance to the journal's readership

- May include only one illustration or table
- Must include a correspondence address.

Obituaries

Guideline word limit: 400 words

Should be offered within the first year of the practitioner's death, and may be accompanied by a photograph.

Illustrations/photos/scans

- If illustrations submitted have been published elsewhere, the author(s) should provide evidence of consent to republication obtained from the copyright holder.
- Figures must be numbered in Arabic numerals and referred to in the text e.g. '(Fig. 1)'.
- Each figure must have a caption/legend: Fig. 1. Description (any abbreviations in full).
- All images must be of high enough resolution/quality for print.
- All illustrations (graphs, diagrams, charts, etc.) must be in PDF form.
- Ensure all graph axes are labelled appropriately, with a heading/description and units (as necessary) indicated. Do not include decimal places if not necessary e.g. 0; 1.0; 2.0; 3.0; 4.0 etc.
- Scans/photos showing a specific feature e.g. *Intermediate magnification micrograph of a low malignant potential (LMP) mucinous ovarian tumour. (H&E stain).* –include an arrow to show the tumour.
- Each image must be attached individually as a 'supplementary file' upon submission (not solely embedded in the accompanying manuscript) and named Fig. 1, Fig. 2, etc.

Tables

- Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged.
- Large tables will generally not be accepted for publication in their entirety. Please consider shortening and using the text to highlight specific important sections, or offer a large table as an addendum to the publication, but available in full on request from the author.
- Embed/include each table in the manuscript Word file - do not provide separately as supplementary files.

- Number each table in Arabic numerals (Table 1, Table 2, etc.) consecutively as they are referred to in the text.
- Tables must be cell-based (i.e. not constructed with text boxes or tabs) and editable.
- Ensure each table has a concise title and column headings, and include units where necessary.
- Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc.

Do not: Use [Enter] within a row to make 'new rows':

Rather:

Each row of data must have its own proper row:

Do not: use separate columns for *n* and %:

Rather:

Combine into one column, *n* (%):

Do not: have overlapping categories, e.g.:

Rather:

Use <> symbols or numbers that don't overlap:

References

NB: *Only complete, correctly formatted reference lists in Vancouver style will be accepted. If reference manager software is used, the reference list and citations in text are to be unformatted to plain text before submitting..*

- Authors must verify references from original sources.
- Citations should be inserted in the text as superscript numbers between square brackets, e.g. These regulations are endorsed by the World Health Organization,[2] and others.[3,4-6]
- All references should be listed at the end of the article in numerical order of appearance in the Vancouver style (not alphabetical order).
- Approved abbreviations of journal titles must be used; see the List of Journals in Index Medicus.
- Names and initials of all authors should be given; if there are more than six authors, the first three names should be given followed by et al.
- Volume and issue numbers should be given.
- First and last page, in full, should be given e.g.: 1215-1217 **not** 1215-17.
- Wherever possible, references must be accompanied by a digital object identifier (DOI) link). Authors are encouraged to use the DOI lookup service offered by CrossRef:
  - On the Crossref homepage, paste the article title into the 'Metadata search' box.
  - Look for the correct, matching article in the list of results.
  - Click Actions > Cite
  - Alongside 'url =' copy the URL between { }.
  - Provide as follows, e.g.: https://doi.org/10.7196/07294.937.98x

Some examples:

- *Journal references:* Price NC, Jacobs NN, Roberts DA, et al. Importance of asking about glaucoma. Stat Med 1998;289(1):350-355. http://dx/doi.org/10.1000/hgjr.182
- *Book references:* Jeffcoate N. Principles of Gynaecology. 4th ed. London: Butterworth, 1975:96-101.
- *Chapter/section in a book:* Weinstein L, Swartz MN. Pathogenic Properties of Invading Microorganisms. In: Sodeman WA, Sodeman WA, eds. Pathologic Physiology: Mechanisms of Disease. Philadelphia: WB Saunders, 1974:457-472.
- *Internet references:* World Health Organization. The World Health Report 2002 - Reducing Risks, Promoting Healthy Life. Geneva: WHO, 2002. http://www.who.int/whr/2002 (accessed 16 January 2010).
- Legal references
- Government Gazettes:

  National Department of Health, South Africa. National Policy for Health Act, 1990 (Act No. 116 of 1990). Free primary health care services. Government Gazette No. 17507:1514. 1996.

  In this example, 17507 is the Gazette Number. This is followed by :1514 - this is the notice number in this Gazette.

- Provincial Gazettes:

  Gauteng Province, South Africa; Department of Agriculture, Conservation, Environment and Land Affairs. Publication of the Gauteng health care waste management draft regulations. Gauteng Provincial Gazette No. 373:3003, 2003.

- Acts:

  South Africa. National Health Act No. 61 of 2003.

- Regulations to an Act:

  South Africa. National Health Act of 2003. Regulations: Rendering of clinical forensic medicine services. Government Gazette No. 35099, 2012. (Published under Government Notice R176).

- Bills:

  South Africa. Traditional Health Practitioners Bill, No. B66B-2003, 2006.

- Green/white papers:

  South Africa. Department of Health Green Paper: National Health Insurance in South Africa. 2011.

- Case law:

  Rex v Jopp and Another 1949 (4) SA 11 (N)

  Rex v Jopp and Another: Name of the parties concerned

  1949: Date of decision (or when the case was heard)

  (4): Volume number

  SA: SA Law Reports

  11: Page or section number

  (N): In this case Natal - where the case was heard. Similarly, (C) woud indicate Cape, (G) Gauteng, and so on.

  NOTE: no . after the v

- *Other references (e.g. reports) should follow the same format:* Author(s). Title. Publisher place: Publisher name, year; pages.
- Cited manuscripts that have been accepted but not yet published can be included as references followed by '(in press)'.
- Unpublished observations and personal communications in the text must **not** appear in the reference list. The full name of the source person must be provided for personal communications e.g. '...(Prof. Michael Jones, personal communication)'.