National Institute for Health and Care Excellence

Draft for consultation

Neonatal jaundice: Phototherapy

Clinical Guideline 98.1

Methods, evidence and recommendations

July 2015

Developed by the National Institute for Health and Care Excellence

Disclaimer
Healthcare professionals are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.

Contents

Clinical guidelines update

The NICE Clinical Guidelines Update Team update discrete parts of published clinical guidelines as requested by NICE's Guidance Executive.

Suitable topics for update are identified through the new surveillance programme (see surveillance programme interim guide).

These guidelines are updated using a standing Committee of healthcare professionals, research methodologists and lay members from a range of disciplines and localities. For the duration of the update the core members of the Committee are joined by up to 5 additional members who are have specific expertise in the topic being updated, hereafter referred to as 'topic expert members'. The Committee are also joined by 1 expert witness (no-voting member) to discuss specific area on medical physics.

In this document where 'the Committee' is referred to, this means the entire Committee, both the core standing members and topic expert members.

Where 'standing committee members' is referred to, this means the core standing members of the Committee only.

Where 'topic expert members' is referred to this means the recruited group of members with topic expertise.

All of the core members and the topic expert members are fully voting members of the Committee, except the expert witness.

Details of the Committee membership and the NICE team can be found in appendix A. The Committee members' declarations of interest can be found in appendix B.

1 Summary section

1.1 Update information

The NICE guideline on neonatal jaundice (NICE clinical guideline CG98) was reviewed in May 2014 as part of NICE's routine surveillance programme to decide whether it required updating. The surveillance report identified new evidence relating to two areas of the guidance:

1) The best modality of giving phototherapy
2) The correct procedure of administering phototherapy

The review questions that the Committee considered were:

1) What is the best modality of giving phototherapy (clinical and cost-effectiveness)?
2) What is the correct procedure when administering phototherapy?

The original guideline can be found here: http://www.nice.org.uk/guidance/cg98

The full surveillance report can be found here:

http://www.nice.org.uk/guidance/cg98/documents/cg98-neonatal-jaundice-surveillance-review-decision2

Strength of recommendations

Some recommendations can be made with more certainty than others. The Committee makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the Committee is confident that, given the information it has looked at, most people would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

For all recommendations, NICE expects that there is discussion with the person about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision (see also 'Patient-centred care').

Recommendations that must (or must not) be followed

We usually use 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally we use 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Recommendations that should (or should not) be followed– a 'strong' recommendation

We use 'offer' (and similar words such as 'refer' or 'advise') when we are confident that, for the vast majority of people, following a recommendation will do more good than harm, and be cost effective. We use similar forms of words (for example, 'Do not offer…') when we are confident that actions will not be of benefit for most people.

Recommendations that could be followed

We use 'consider' when we are confident that following a recommendation will do more good than harm for most people, and be cost effective, but other options may be similarly cost effective. The course of action is more likely to depend on the person's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the person.

Information for consultation

You are invited to comment on the new and updated recommendations in this guideline. These are marked as:

- **[new 2015] if the evidence has been reviewed and the recommendation has been added or updated**
- **[2015] if the evidence has been reviewed but no change has been made to the recommended action.**

You are also invited to comment on recommendations that NICE proposes to delete from the 2010 guideline, because either the evidence has been reviewed and the recommendations have been updated, or NICE has updated other relevant guidance and has replaced the original recommendations. Appendix A sets out these recommendations and includes details of replacement recommendations. Where there is no replacement recommendation, an explanation for the proposed deletion is given.

Where recommendations are shaded in grey and end [2010], the evidence has not been reviewed since the original guideline. We will not be able to accept comments on these recommendations. Yellow shading in these recommendations indicates wording changes that have been made for the purposes of clarification only.

1.21 Recommendations

This addendum only updates recommendations 1.4.9 to 1.4.13, and 1.4.18 to 1.4.19 of CG98.

Type of phototherapy to use

1. **Do not use sunlight as treatment for hyperbilirubinaemia. [2010]**

2. **Use phototherapy[a] to treat significant hyperbilirubinaemia (see threshold table and treatment threshold graphs[4]) in babies [new 2015]**

3. **Consider intensified phototherapy[c] to treat significant hyperbilirubaemia in babies if any of the following apply [new 2015]:**
   - **the serum bilirubin level is rising rapidly (more than 8.5 micromol/litre per hour)**
   - **the serum bilirubin is at a level within 50 micromol/litre below the threshold for which exchange transfusion is indicated after 72 hours (see threshold table and treatment threshold graphs[4])**
   - **the bilirubin level fails to respond to initial phototherapy (that is, the level of serum bilirubin continues to rise, or does not fall, within 6 hours of starting phototherapy. [2010]**

4. **If the serum builirubin level falls during the intensified phototherapy to a level of 50 micromol/litre below the threshold for which exchange transfusion is indicated, reduce the intensity of phototherapy. [2010]**

Monitoring the baby during phototherapy

5. **During phototherapy[a]:**
   - **using clinical judgement, encourage short breaks (of up to 30 minutes) for breastfeeding, nappy changing and cuddles**
   - **continue lactation/feeding support**
   - **do not give additional fluids or feeds routinely**

   Maternal expressed milk is the additional feed of choice if available, and when additional feeds are indicated. [2015]
   -

6. **During intensified phototherapy[b]:**
   - **do not interrupt phototherapy for feeding but continue administering intravenous/enteral feeds**
   - **continue lactation/feeding support so that breastfeeding can start again when treatment stops.**

   Maternal expressed milk is the additional feed of choice if available, and when additional feeds are indicated. [2015]

Definition:
[a] Phototherapy given using artificial light sources with appropriate spectrum and irradiance. This can be delivered by light-emitting diode (LED), fibreoptic or fluorescent lamps or tubes or bulbs.
[4] The management of hyperbilirubinaemia is detailed in another section of the full guideline named: Threshold table. Consensus-based bilirubin thresholds for management of babies 38 weeks or more gestational age with hyperbilirubinaemia
[b] Phototherapy that is given with an increased level of irradiance with an appropriate spectrum. Phototherapy can be intensified by adding another light source or increasing the irradiance of the initial light source used.

1.3 Patient-centred care

This guideline offers best practice advice on the care newborn babies with jaundice.

Patients and healthcare professionals have rights and responsibilities as set out in the NHS Constitution for England – all NICE guidance is written to reflect these. Treatment and care should take into account individual needs and preferences. Patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If the person is under 16, their family or carers should also be given information and support to help the child or young person make decisions about their treatment. Healthcare professionals should follow the Department of Health's advice on consent. If someone does not have the capacity to make decisions, healthcare professionals should follow the code of practice that accompanies the Mental Capacity Act and the supplementary code of practice on deprivation of liberty safeguards. In Wales, healthcare professionals should follow advice on consent from the Welsh Government.

1.4 Methods

This update was developed based on the process and methods described in the The Manual 2014 (but the development of the review protocol followed The Guideline Manual 2012). Where there are deviations from the process and methods, these are clearly stated in the interim process and methods guide for updates pilot programme 2013.

2 Evidence review and recommendations

2.1 Introduction

Jaundice is one of the most common conditions requiring medical attention in newborn babies. Jaundice refers to the yellow colouration of the skin and sclera (whites of the eyes) resulting from the accumulation of bilirubin in the skin and mucous membranes. This is associated with a raised level of bilirubin in the circulation, a condition known as hyperbilirubinaemia.

Levels of bilirubin can be controlled by placing the baby under a lamp emitting light in a particular spectrum, which is known as phototherapy. Light energy of the appropriate wavelength converts the bilirubin in the skin to a form that can be excreted in the urine. Phototherapy has proved to be a safe and effective treatment for jaundice in newborn babies, reducing the need to perform an exchange transfusion of blood, the only other means of removing bilirubin from the body.

Traditional teaching on examination for jaundice has recommended 'blanching' a small area of skin (often on the nose) by pressing it, and inspecting the whites of the eyes and palate. Jaundice is also thought to spread from the head to the toes in a 'cephalo-caudal' progression. Given the difficulty involved in making a diagnosis, one of the aims of this update is to address the accuracy of various tests used to recognise neonatal jaundice or hyperbilirubinaemia.

2.2 Review question 1

What is the best modality of giving phototherapy (clinical and cost-effectiveness)?

2.3 Clinical evidence review

Phototherapy is considered to be an effective treatment for jaundice in neonates. However, there is uncertainty on which is the best modality (for example, light from LED, fiberoptic or fluorescent lamps/tubes/bulbs) of giving phototherapy. The aim of this review therefore is to evaluate the best modality of giving phototherapy.

An update search using the original search strategy was conducted (see appendix D) which identified 827 articles (for both review question 1 and 2). The titles and abstracts were screened and 110 articles were identified as potentially relevant. Full-text versions of these 110 articles were obtained and reviewed against the criteria specified in the review protocol (appendix C). Of these, 97 were excluded as they did not meet the criteria. 13 studies (question 1 = 5; question 2 = 8) met the inclusion criteria and were included with an additional 24 studies (question 1 = 12; question 2 = 12) from CG98. Therefore, a total of 37 studies are included (question 1 = 17; question 2 = 20) for this update with:

Review question 1: 17 studies (5 new, 12 old)

Review question 2: 20 studies (8 new, 12 old)

Note: old refers to studies included in the original guideline; new refers to studies included in this update.

A review flowchart is provided in appendix E and the list of excluded studies (with reasons for exclusion) are shown in appendix F.

2.3.1 Methods

Summary of review protocols

For review question 1, the population included newborns with a diagnosis of jaundice but who were otherwise well. The subgroup of preterm infants was also identified.

The intervention of interest was conventional phototherapy (single, double or multiple phototherapy using fluorescent tubes or bulbs) compared against the following comparators (data on any comparisons as opposed to specific pair-wise comparisons were to be analysed):

- sunlight
- fibreoptic phototherapy (biliblankets, bilibeds and other products)
- LED phototherapy (LED spot lights)
- LED phototherapy (LED pads)

The topic experts outlined the following outcomes as:

Important outcomes:

- Number of exchange transfusions
- Treatment failure (as defined in the study) including cases of rebound jaundice and kernicterus
- Mean duration of phototherapy
- Staff experience
- Adverse events of phototherapy including mortality

Critical outcomes:

- Mean change in serum bilirubin and rate of decline of bilirubin
- Parental experience/acceptability including access for bonding and breastfeeding
- incidence/odds of developing IE in those receiving prophylaxis compared to those not receiving prophylaxis and incidence of adverse effects including anaphylaxis

GRADE methodology was used to assess the quality of evidence as follows:

Risk of bias:

As only RCTs were included in this review, criteria suggested by the GRADE methodology (http://www.gradeworkinggroup.org/) were used for assessing risk of bias.

Indirectness:

Details from the PICOs in the review protocol(s) (see appendix C) were used to assess the directness of the included studies.

Inconsistency:

Where meta-analysis was conducted, consistency was assessed as follow:

- For fixed effects model: if I^2 >50% with Chi^2 p <0.1, sensitivity analysis would be conducted to explore clinical heterogeneity. If no clinical heterogeneity was identified, more conservative random effects model would be used and the corresponding outcome would be downgraded 1 level.
- For random effects model: if Tau^2 >1.00, downgrade 1 level.

Imprecision:

A routine search of the COMET (Core Outcome Measures in Effectiveness Trials) Initiative database was conducted to identify any relevant thresholds for defining the clinical minimal important difference (MIDs). No information was identified in the COMET database. Information about specific MIDs used to assess imprecision were also not available from the original guideline CG98. The topic experts were consulted on the MIDs particularly for continuous outcomes such as mean duration of phototherapy (hours) and total serum bilirubin level (TSB). The topic experts felt that it was very challenging and possibly inappropriate to set arbitratry thresholds for these continuous outcomes due to the following reasons:

- excretion of excess bilirubin is non-linear, and the pattern of falling bilirubin concentrations with time is also non-linear. This non-linearity interacts with infant's gestational age, age at initiation of phototherapy, and the baseline TSB at the initiation of phototherapy.
- there are significant intra-individual variations (same value of TSB can have a very different clinical importance in different infants hence it is difficult to give a particular rate of reduction of TSB and pthototherapy duration).

Due to the above difficulties, the following universal/default thresholds were used to assess the precision of effect estimates:

- For continuous outcomes: a threshold of sample size ≥400 would be used to assess 'imprecision' (based on α (0.05) and β (0.20), and an effect size of 0.2 standard deviations), as recommended by the GRADE Working Group.
- For dichotomous outcomes: RRR or RRI of 25%: 0.75 or 1.25 (as recommended by the GRADE Working Group).

Where the universal/default thresholds are not appropriate for certain outcomes (e.g. mortality), further discussion would take place and would be documented in the LETR table.

Overall quality:

As only RCTs were included for this systematic review, the quality rating of outcomes began at 'high' and then further downgraded for potential sources of bias (if any) accordingly.

Statistical analysis:

Where appropriate, meta-analyses were conducted using Review Manager 5.3

Overall summary of evidence

Overall, the majority of the evidence was of low to very quality because most included did not report method of randomisation, or have unclear allocation concealment, or both. Moreover, the majority of the included studies have very small sample size, pooling the data with meta-analysis did not substantially increase the sample size. Due to the nature of the treatment, studies with no blinding were not downgraded.

For a summary of included studies please see table 1 below (for the full evidence tables please see appendix G, full GRADE profiles please see appendix H, and for forest plots please see appendix I).

1 **Table 1: Summary of included studies – Review question 1**

Study reference (including study design)	Study population	Intervention & comparator	Outcomes reported	Comments
Conventional phototherapy vs. LED Phototherapy				
Demirel (2010) RCT	Term infants Mean age at PT = 71 hours Baseline mean TSB = 308 umol/L	Conventional phototherapy vs. LED Phototherapy	• Mean duration of phototherapy (hours)	Conventional: AMS Phototherapy System (consisting of 6 fluorescent lamps) LED: Blue LED (neoBLUE® LED phototherapy system, Natus Medical, San Carlos, CA)
Kumar (2010) RCT	Term infants Mean age at PT = 82 hours Baseline mean TSB = 288 umol/L	Conventional phototherapy vs. LED Phototherapy	• Median duration of phototherapy (hours) • Mean decrease of TSB per hour of PT(umol/L/hour) • Failure of phototherapy • Exchange transfusion • Rebound jaundice	Conventional: CFT units consisting of 6 special blue compact fluorescent bulbs (18W, OSRAM special blue lamp) LED: LED phototherapy units (Srichakra Scientifics, Hyderabad)
Ngerncham (2012) RCT	Term infants Mean age at PT = 69 hours Baseline median TSB = 244 umol/L	Conventional phototherapy vs. LED Phototherapy	• Median duration of phototherapy (hours) • Rebound jaundice	Conventional: 6 special blue fluorescent tubes (“Deep blue”, Thai Toshiba Electric Company, 18 watts) LED: the Bilitron 3006 (Fanem, Sao Paulo, Brazil) with 5 super LEDs
Seidman (2000) RCT	Term infants Mean age at PT = Not reported Baseline mean TSB = 251 umol/L	Conventional phototherapy vs. LED Phototherapy	• Mean duration of phototherapy (hours) • Mean decrease in TSB per hour of PT (umol/L/hour)	Conventional: Halogen-quartz bulbs (Micro-lites PTL 68–1) LED: 6 x 100 3-mm blue LED (Christopher A. Julian of Intuitive Machine Design, Los Gatos, California).
Seidman (2003)	Term infants	Conventional	• Mean duration of phototherapy	Conventional: Halogen-quartz bulbs (Micro-

Study reference (including study design)	Study population	Intervention & comparator	Outcomes reported	Comments
RCT	Mean age at PT = 52 hours Baseline mean TSB = 250 umol/L	phototherapy vs. LED Phototherapy (blue or blue-green)	(hours) • Mean decrease in TSB per hour of PT (umol/L/hour)	lites PTL 68–1) LED: custom built at the Standard University. For blue: 6 x 100 3-mm (NSPB-500S, Nichia Chemical Industries Ltd) For blue: 6 x 100 3-mm (NSPB-590S, Nichia Chemical Industries Ltd)
Bertini (2008) RCT	Preterm infants Mean age at PT = 64 hours Baseline mean TSB ≥ 171 umol/L	Conventional phototherapy vs. LED Phototherapy	• Mean duration of phototherapy (hours) • Transepidermal water loss (TEWL) after 12-24 hrs of phototherapy (ml/m^2/hour)	Conventional: Blue burb (Photo-Therapie 800) LED: Blue LED (Natus NeoBlue system)
Martins (2007) RCT	Preterm infants Mean age at PT = 68 hours Baseline TSB unclear.	Conventional phototherapy vs. LED Phototherapy	• Mean duration of phototherapy (hours) • Rebound jaundice	Conventional: Single halogen-quartz lamp LED: Super LED system
Surmeli-Onay (2013) RCT	Preterm infants Mean age at PT = 66 hours Baseline mean TSB = 146 umol/L	Conventional phototherapy vs. LED Phototherapy	• Mean duration of phototherapy (hours) • Skin eruption • All-cause mortality	Conventional: 2 white lamps (Ertunc Ozcan IC100 Phototherapy device) LED: Blue LED (neoBLUE® LED phototherapy system, Natus Medical, San Carlos, CA)
Viau-Colindres (2012) RCT	Preterm infants Mean age at PT = Not reported Baseline mean TSB = 205	Conventional phototherapy vs. LED Phototherapy	• Mean duration of phototherapy (hours) • Mean decrease in TSB per hour of PT (umol/L/hour) • (no SD provided for both outcomes, only the p-value)	Conventional: Blue fluorescent (6 x Medix phototherapy lamp, model LU-6T, S|N 568-06) or Halogen (3 x Air Shields Micro-lite model PPT 68-1, series 2) LED: Researcher self-made LED panel with

Study reference (including study design)	Study population	Intervention & comparator	Outcomes reported	Comments
	umol/L			80 x 10mm blue LEDs.
Conventional phototherapy vs. Fiberoptic phototherapy				
Gale (1990) RCT	Term infants Mean age at PT = Not reported Baseline mean TSB = 186.5 umol/L	Conventional phototherapy vs. Fiberoptic phototherapy	• Mean decrease in TSB after 48 hrs of PT (umol/L)	Conventional: Air Shields PT 53–3 consisted of both daylight and blue lamps. Fiberoptic: Wallaby Phototherapy System (Fiberoptic Medical Products Inc. USA)
Pezzati (2002) RCT	Term infants Mean age at PT = Not reported Baseline mean TSB = 294.5 umol/L	Conventional phototherapy vs. Fiberoptic phototherapy	• Mean skin temperature during phototherapy (degree Celsius) for forehead, abdomen, left leg and back.	Conventional: Photo-Therapie 800 system, Drager, Germany. Fiberoptic: Biliblanket (Bili-Blanket, Ohmeda, USA).
Sarici (2001) RCT	Term infants Mean age at PT = 105.4 hours Baseline mean TSB = 307.5 umol/L	Conventional phototherapy vs. Fiberoptic phototherapy	• Mean duration of phototherapy (hours) • Mean decrease in TSB per hour (in %/hour) • Rebound jaundice • Treatment failure (needing double phototherapy) • Erythema • Watery stools	Conventional: 5 daylight fluorescent lamps (Ohio Medical Products) Fiberoptic: Wallaby II Phototherapy System (Fiberoptic Medical Products Inc. USA)
Costello (1995) RCT	Preterm infants Mean age at PT = 56 hours Baseline mean TSB = not reported.	Conventional phototherapy vs. Fiberoptic phototherapy	• Mean duration of phototherapy (hours) • Treatment failure (need double phototherapy)	Conventional: standard system of four white and 4 blue fluorescent lamps. Fiberoptic: Biliblanket (Bili-Blanket, Ohmeda, USA).

Study reference (including study design)	Study population	Intervention & comparator	Outcomes reported	Comments
Dani (2004) RCT	Preterm infants Mean age at PT = 63 hours Baseline mean TSB = 242 umol/L	Conventional phototherapy vs. Fiberoptic phototherapy	• Mean duration of phototherapy (hours) • Mean skin temperature 24-36 hours of PT (degree Celsius)	Conventional: Photo-Therapie 800 system, Drager, Germany. Fiberoptic: Biliblanket (Bili-Blanket, Ohmeda, USA).
Romagnoli (2006) RCT	Preterm infants Mean age at PT = 38 hours Baseline mean TSB = 109.5 umol/L	Conventional phototherapy vs. Fiberoptic phototherapy	• Mean duration of phototherapy (hours) • Mean decrease in TSB from baseline after 48-72 hours (in %) • Exchange transfusion • Erythema	Conventional: 4 fluorescent lamps (True light, Duro Test, 20TH12TXC) and 4 blue lamps (Philips TL20W/03T). Fiberoptic: Wallaby II Phototherapy System (Fiberoptic Medical Products Inc. USA) or Biliblanket (Bili-Blanket, Ohmeda, USA).
Van Kaam (1998) RCT	Preterm infants Mean age at PT = 26.5 hours Baseline mean TSB = 94 umol/L	Conventional phototherapy vs. Fiberoptic phototherapy	• Mean duration of phototherapy (hours) • Exchange transfusion • All-cause mortality	Conventional: 4 fluorescent lamps (Philips TLK 40W/03) Fiberoptic: Biliblanket (Bili-Blanket, Ohmeda, USA).
Conventional phototherapy vs. Conventional + Fiberoptic phototherapy				
Holtrop (1992) RCT	Preterm infants Mean age at PT = 58 hours Baseline mean TSB = Not reported	Conventional phototherapy vs. Conventional + Fiberoptic phototherapy	• Mean decrease in TSB from baseline after 18 hours (in %) • Mean decrease in TSB from baseline after 18 hours (umol/L) • Rebound jaundice	Conventional: 5 daylight fluorescent lamps (Ohio Medical Product) Fiberoptic: Wallaby II Phototherapy System (Fiberoptic Medical Products Inc. USA)
Romagnoli (2006)[a] RCT	Preterm infants Mean age at PT = 38 hours	Conventional phototherapy vs. Conventional + Fiberoptic phototherapy	• Mean duration of phototherapy (hours) • Mean decrease in TSB from baseline after 48-72 hours (in %)	Conventional: 4 fluorescent lamps (True light, Duro Test, 20TH12TXC) and 4 blue lamps (Philips TL20W/03T).

Study reference (including study design)	Study population	Intervention & comparator	Outcomes reported	Comments
	Baseline mean TSB = 109.5 umol/L		• Exchange transfusion • Erythema	Fiberoptic: Wallaby II Phototherapy System (Fiberoptic Medical Products Inc. USA) or Biliblanket (Bili-Blanket, Ohmeda, USA).

(a) Romagnoli (2006) – Multi-arms trial
PT = phototherapy; TSB = total serum bilirubin

2.41 Health economic evidence, review question 1

2.4.12 Methods

3 Evidence of cost effectiveness

4 The Committee is required to make decisions based on the best available evidence of both
5 clinical and cost effectiveness. Guideline recommendations should be based on the expected
6 costs of the different options in relation to their expected health benefits rather than the total
7 implementation cost.

8 Evidence on cost effectiveness related to the key clinical issues being addressed in the
9 guideline update was sought. The health economist undertook a systematic review of the
10 published economic literature.

11 Economic literature search

12 A systematic literature search was undertaken to identify health economic evidence within
13 published literature relevant to the review questions 1 and 2. The evidence was identified by
14 conducting a broad search relating to phototherapy in the NHS Economic Evaluation
15 Database (NHS EED) and the Health Technology Assessment database (HTA). The search
16 also included Medline and Embase databases using an economic filter combined with the
17 clinical search terms. Studies published in languages other than English were not reviewed.
18 The search was conducted on 18 March 2015. The health economic search strategies are
19 detailed in appendix J.

20 The health economist also sought out relevant studies identified by the surveillance review or
21 Committee members.

22 Economic literature review

23 The health economist:

24 • Identified potentially relevant studies for each review question from the economic search
25 results by reviewing titles and abstracts. Full papers were then obtained.
26 • Reviewed full papers against prespecified inclusion and exclusion criteria to identify
27 relevant studies.

28 Inclusion and Exclusion criteria

29 Full economic evaluations (studies comparing costs and health consequences of alternative
30 courses of action: cost-utility, cost-effectiveness, cost-benefit and cost-consequence
31 analyses) and comparative costing studies that address the review question in the relevant
32 population were considered potentially includable as economic evidence. Studies that only
33 reported burden of disease or cost of illness were excluded. Literature reviews, abstracts,
34 posters, letters, editorials, comment articles, unpublished studies and studies not in English
35 were excluded.

36 Remaining studies were prioritised for inclusion based on their relative applicability to the
37 development of this guideline and the study limitations. For example, if a high quality, directly
38 applicable UK analysis was available, then other less relevant studies may not have been
39 included. Where selective exclusions occurred on this basis, this is noted in the excluded
40 economic studies table (appendix L).

For more details about the assessment of applicability and methodological quality see the economic evaluation checklist contained in *Appendix H* of *Developing NICE Guidelines: the manual 2014*.

Cost-effectiveness criteria

NICE's report *Social value judgements: principles for the development of NICE guidance* sets out the principles that GDGs should consider when judging whether an intervention offers good value for money. In general, an intervention was considered to be cost effective if either of the following criteria applied (given that the estimate was considered plausible):

- the intervention dominated other relevant strategies (that is, it was both less costly in terms of resource use and more clinically effective compared with all the other relevant alternative strategies), or
- the intervention cost less than £20,000 per QALY gained compared with the next best strategy.

If the Committee recommended an intervention that was estimated to cost more than £20,000 per QALY gained, or did not recommend one that was estimated to cost less than £20,000 per QALY gained, the reasons for this decision are discussed explicitly in the 'evidence to recommendations' section of the relevant chapter, with reference to issues regarding the plausibility of the estimate or to the factors set out in *Social value judgements: principles for the development of NICE guidance*.

In the absence of economic evidence

When no relevant economic studies were found from the economic literature review, and de novo modelling was not feasible or prioritised, the Committee made a qualitative judgement about cost-effectiveness by considering expected differences in resource use between options and relevant UK NHS unit costs, alongside the results of the clinical review of effectiveness evidence. The UK NHS costs reported in the guideline were those presented to the Committee and they were correct at the time recommendations were drafted; they may have been revised subsequently by the time of publication. However, we have no reason to believe they have been changed substantially.

2.4.2 Results of the economic literature review, review question 1

169 articles were identified by the initial combined search for review questions 1 and 2. 162 of these were excluded based on the title of the article and abstract. Seven articles were selected for consideration of the full version. Three of these could not be obtained and the other 4 were excluded. The flowchart summarising this review process can be found in appendix K. The list of excluded studies and the reasons for their exclusion can be found in appendix L.

2.4.3 Cost of phototherapy

The cost of conventional phototherapy units could not be identified. Costs were identified at a local level for one brand of LED phototherapy devices as per Table 2. The LED light box is expected to be replaced every 3000 hours of operation or every 18 to 24 months. Expert advice was that conventional fluorescent tubes or bulbs need to be replaced every 12 months and conventional phototherapy devices are, in general, more costly than LED devices.

Table 2: LED device costs

Device	Cost
neoBLUE LED Phototherapy System	£2,800

Device	Cost
neoBLUE cozy LED Phototherapy System	£2,200
neoBLUE blanket LED Phototherapy System	£2,300
neoBLUE mini LED Phototherapy System	£2,300
neoBLUE light bulb box (replacement)	£1,500

2.5 Evidence statements

2.5.1 Clinical evidence statement

Conventional phototherapy compared with LED phototherapy

9 RCTs (N = ranged from 31 to 272) suggested that there was no clear evidence of differences between conventional phototherapy and LED phototherapy for the following outcomes: mean duration of phototherapy, mean decrease in TSB per hour, rebound jaundice, skin eruption, exchange transfusion and all-cause mortality, for term and preterm babies. (moderate to very low quality)

1 small RCT (N = 31) suggested that pre-term infants under the treatment of LED phototherapy had significantly less transepidemal water loss compared to preterm infants under conventional phototherapy. (low quality)

Conventional phototherapy compared with fiberoptic phototherapy

Overall, for both term and pre-term babies, 4 RCTs (N = ranged from 23 to 103) suggested that there was no clear evidence of differences between conventional phototherapy and fiberoptic phototherapy for mean duration of photherapy, treatment failure and erythema. (low to very low quality)

Another 7 RCTs (N = ranged from 41 to 124) suggested that there was no clear evidence of differences between conventional phototherapy and fiberoptic phototherapy for the following outcomes: mean decrease in TSB from baseline after 48 to 72 hours, rebound jaundice, exchange transfusion, treatment failure, erythema, all-cause mortality, watery stools, and skin temperature (left leg and back) for term and preterm babies. (low to very low quality)

1 RCT (N = 100) suggested that term babies under conventional phototherapy had shorter mean duration of phototherapy with greater mean decrease in TSB per hour compared to term infants under fiberoptic phototherapy (low quality). However, 3 RCTs (N = ranged from 23 to 103 suggested that preterm babies under fiberoptic phototherapy had shorter mean duration of phototherapy compared to preterm infants under conventional phototherapy (low quality). Another small RCT (N = 41) also suggested that term babies under fiberoptic phototherapy had lower skin temperature (forehead and abdomen) compared to preterm babies under conventional phototherapy (low quality).

Conventional phototherapy compared with conventional phototherapy plus fiberoptic phototherapy

2 small RCTs (N = 70 and 66) suggested that babies under dual phototherapy (conventional plus fiberoptic) had greater mean decrease of TSB (term and preterm babies) and shorter mean duration of phototherapy (pre-term babies only) compared to conventional phototherapy alone. The same 2 RCTs also suggested that there was no clear evidence of differences for rebound jaundice, exchange transfusion and erythema between the 2 interventions. (low to very low quality)

No included studies reported staff experience and parental experience/acceptability as study outcomes.

2.5.23 Health economic evidence statements

No studies were included in the economic literature review.

2.65 Evidence to recommendations

	Committee discussions
Relative value of different outcomes	The committee discussed the evidence and agreed that the three most important outcomes are the rate of decrease of serum bilirubin, adverse effects of phototherapy particularly transepidemal water loss or dehydration, and experiences of parents and staff. The committee acknowledged that no evidence identified reported experiences of parents and/or staff. The committee stated that this could be a very useful surrogate outcome for assessing how distressed or comfortable babies are when they are under phototherapy. The committee also commented about parents' experience, the distress to parents of their babies being removed from home and hospitalised for treatment and the impact of this on their bonding with babies. The committee further noted that mean duration of phototherapy is only a surrogate outcome of efficiency of phototherapy and not a very precise outcome on which to base a decision. The topic experts explained that the actual spectrum of light and levels of irradiance are directly related to the rate of decrease of serum bilirubin, not just the overall modality of light sources used (e.g. fluorescent, LED or fiberoptic) as each of these modality of light sources has a different spectrum and could be set to varying degrees of irradiance (for example, a fluorescent lamp device or a LED device itself can be set to certain light spectrum and irradiance, as well as varying them accordingly). Therefore, simply comparing the overall modality of light sources without comparing the actual spectrum and irradiance used in those studies would not give a clear picture of efficacy. Unfortunately, none of the current available evidence was designed to appropriately compare: light source/spectrum/irradiance vs. another light source/spectrum/irradiance. All current identified evidence only compared the modality of light sources without adjusting the spectrum and irradiance used. The committee felt that current evidence is unclear to suggest any differences on these outcomes simply by the modality of light sources.
Quality of evidence	The committee agreed that the majority of evidence was of low to very low quality due to study design issues (unclear randomisation methods and allocation concealment) and small sample size. These factors have increased their uncertainty in drawing any conclusion that there are differences between different light sources for either term or preterm babies.
Trade-off between benefits and harms	The committee agreed with the assumption that phototherapy is an effective treatment for neonatal jaundice by reducing the serum bilirubin. However, based on the evidence and its quality, the committee could not confidently draw any conclusion on which light sources (modality) have better outcomes, either beneficial or harmful outcomes, for both term and preterm babies. The committee agreed that phototherapy should be recommended for all neonatal babies with jaundice, but they could not specify which specific modality is best based on current evidence.

	Committee discussions
	The committee discussed the limited low to very low quality evidence on single phototherapy vs multiple phototherapy (i.e. conventional phototherapy vs conventional + fiberoptic phototherapy) and agreed that current evidence supports the original recommendation that multiple phototherapy would be beneficial for babies whom serum bilirubin rose rapidly within short period of time, or if the initial phototherapy failed to reduce the level of serum bilirubin. However, based on the very limited and low to very low quality of the evidence, the committee felt that the recommendation should be updated to 'consider' from 'offer' due to the uncertainty of the evidence. The topic experts explained that multiple phototherapy is superior to single phothotherapy due to more light sources that increase the level of irradiance. The topic experts noted that with modern devices now this could be achieved by simply adjusting the level of irradiance in a device without adding additional devices to the treatment. Therefore, the committee overall agreed that due to the progress of modern devices since the original guideline was published, the term 'multiple phototherapy' is no longer relevant to current practice and that it should be edited to 'intensified phototherapy', emphasising the increase of irradiance rather than the number of devices.
Trade-off between net health benefits and resource use	No economic studies were identified that compared the cost effectiveness of different types of phototherapy. The cost of conventional phototherapy devices could not be established because they could not be identified in the NHS Supply Chain database and topic experts advised that they no longer purchased them. The cost of one brand of LED devices was considered by the committee because they could not be identified in the NHS Supply Chain database and it was the only pricing that topic experts provided. Although the cost difference between modalities could not be established, topic experts advised the committee that LED devices cost less than conventional phototherapy units based on their estimates of the cost of the initial purchase of devices, maintenance costs and electricity costs. The Committee decided that one type of phototherapy could not be preferred to another based on economic factors alone.
Other considerations	The topic experts also informed the standing committee members about their experiences of current practice; most neonatal units are now using LED or fiberoptic devices because they produce less glare, generate less heat, are smaller and easier to use, and only need their bulbs changed once every 2 years (compared to every year for fluorescent tubes/lamps). There are only a small number of neonatal units in the UK that still use conventional fluorescent devices because they are still operational and unbroken (with no clear evidence that they are inferior), and replacing them with LED or fiberoptic will have huge resource burden on the NHS. However, the topic experts believed that in the next few years fluorescent devices will be phased out and replaced by LED or fiberoptic because of the above reasons. Overall, the committee agreed that phototherapy is effective for treating jaundice in term and preterm babies. However, based on the uncertainty of the evidence, they could not recommend a specific modality of phototherapy.

2.7 Recommendations

Type of phototherapy to use

1. Do not use sunlight as treatment for hyperbilirubinaemia. [2010]

2. Use phototherapy[a] to treat significant hyperbilirubinaemia[4] (see threshold table and treatment threshold graphs[4]) in babies [new 2015}

3. Consider intensified phototherapy[c] to treat significant hyperbilirubinaemia in babies if any of the following apply [new 2015]:

- the serum bilirubin level is rising rapidly (more than 8.5 micromol/litre per hour)
- the serum bilirubin is at a level within 50 micromol/litre below the threshold for which exchange transfusion is indicated after 72 hours (see threshold table and treatment threshold graphs[[4]])
- the bilirubin level fails to respond to initial phototherapy (that is, the level of serum bilirubin continues to rise, or does not fall, within 6 hours of starting phototherapy. [2010]

4. If the serum builirubin level falls during the intensified phototherapy to a level of 50 micromol/litre below the threshold for which exchange transfusion is indicated, reduce the intensity of phototherapy. [2010]

Definition:

[a] Phototherapy given using artificial light sources with appropriate spectrum and irradiance. This can be delivered by light-emitting diode (LED), fibreoptic or fluorescent lamps or tubes or bulbs.

[4] The management of hyperbilirubinaemia is detailed in another section of the full guideline named: Threshold table. Consensus-based bilirubin thresholds for management of babies 38 weeks or more gestational age with hyperbilirubinaemia

[c] Phototherapy that is given with an increased level of irradiance with an appropriate spectrum. Phototherapy can be intensified by adding another light source or increasing the irradiance of the initial light source used.

2.8[4] Research recommendations

No research recommendation was identified.

2.9 Review question 2

What is the correct procedure of giving phototherapy?

2.10 Clinical evidence review

The aim of this systematic review is to evaluate the correct procedure of giving phototherapy. As this question is related to review question 1, all evidence regarding procedure of giving phototherapy (regardless of the modality of phototherapy) that met the inclusion criteria based on the review protocol (appendix C) was summarised for discussion.

The update search and selection process were the same as described in section 2.3. A total of 37 studies are included (question 1 = 17; question 2 = 20) for this update with:

Review question 1: 17 studies (5 new, 12 old)

Review question 2: 20 studies (8 new, 12 old)

Note: old refers to studies included in the original guideline; new refers to studies included in this update.

A review flowchart is provided in appendix E and the list of excluded studies (with reasons for exclusion) are shown in appendix F.

2.10.1 Methods

Summary of review protocols

For review question 2, the population included newborns with a diagnosis of jaundice but otherwise well. The subgroup of preterm infants was also identified.

The interventions of interest included:

- Fixed position
- Eye coverings
- Intermittent feeds (brief interruptions of phototherapy treatment to facilitate breastfeeding and cuddles)
- Curtains
- Incubators/bassinets
- Bulb colour
- Size of fibreoptic pads (small vs large)
- Light intensity/distance of phototherapy device

The above interventions were compared against the following comparators (data on any comparisons as opposed to specific pair-wise comparisons were to be analysed:

- Changing position
- No/other types of eye coverings
- Continuous feeds/breast/bottle/nasogastric tube feeding
- No curtains
- No incubators/bassinets
- Different bulb colour
- Different sized pad

- Different light intensity/distance of phototherapy device

The topic experts outlined the following outcomes:

Important outcomes:

- Mean duration of treatment
- Cases of purulent eye discharge
- Features of conjunctivitis
- Hydration
- Adverse events of phototherapy including mortality

Critical outcomes:

- Mean change in serum bilirubin and rate of decline of bilirubin
- Parental experience/acceptability including access for bonding and breastfeeding

GRADE methodology was used to assess the quality of evidence as follows:

Same criteria and principles were used as in review question 1, please see section 2.3.1.

Overall quality:

Same as review question 1, please section 2.3.1.

Statistical analysis:

Same as review question 1, please section 2.3.1.

Overall summary of evidence

Same as review question 1, please section 2.3.1.

For a summary of included studies please see table 4 below (for the full evidence tables please appendix G, for the full GRADE profiles please see appendix H ,and for the forest plots please see appendix I).

Table 3: Summary of included studies – Review question 2

Study reference (including study design)	Study population	Intervention & comparator	Outcomes reported	Comments
Colour of light burbs/lamps				
Amato (1991) RCT	Term infants Mean age at PT = 70.5 hours Baseline mean TSB = Not reported	Conventional PT-Blue vs Conventional PT-Green	• Mean duration of PT (hours) • Mean decrease in TSB from baseline at 24 hours (umol/L)	Blue fluorescent (Philips TL/20W/52) and green fluorescent lamps (Sylvania F20T12G)
Ayyash (1987) RCT	Term infants Mean age at PT = 59.7 hours Baseline mean TSB = 283 umol/L	Conventional PT-Blue vs Conventional PT-Green	• Mean duration of PT (hours) • Mean decrease in TSB per hour (umol/L/hour)	Blue fluorescent (Sylvania F20T12B) and green fluorescent lamps (Sylvania F20T12G)
Ayyash (1987a) RCT	Term infants Mean age at PT = 102 hours Baseline mean TSB = 286 umol/L	Conventional PT-Blue vs Conventional PT-Green	• Mean duration of PT (hours) • Mean decrease in TSB per hour (umol/L/hour)	5 blue fluorescent (Sylvania F20T12B) and 5 green fluorescent lamps (Sylvania F20T12G)
Seidman (2003) RCT	Term infants Mean age at PT = 52 hours Baseline mean TSB = 250 umol/L	LED PT-Blue vs LED PT-Blue-green	• Mean duration of phototherapy (hours) • Mean decrease in TSB per hour of PT (umol/L/hour)	LED: custom built at the Standard University. For blue: 6 x 100 3-mm (NSPB-500S, Nichia Chemical Industries Ltd) For blue: 6 x 100 3-mm (NSPB-590S, Nichia Chemical Industries Ltd)
Ebbesen (2007) RCT	Preterm infants Mean age at PT = 74 hours Baseline mean TSB = 221 umol/L	Conventional PT-Blue vs Conventional PT-Turquoise	• Mean decrease in TSB from baseline at 24 hours (umol/L)	8 blue fluorescent and 8 turquoise fluorescent lamps (Philips TL20W/52)
Ayyash (1987a)[a]	Pre-term infants	Conventional PT-Blue	• Mean duration of PT (hours)	5 blue fluorescent (Sylvania

Study reference (including study design)	Study population	Intervention & comparator	Outcomes reported	Comments
RCT	Mean age at PT = 85.6 hours Baseline mean TSB = 239 umol/L	vs Conventional PT-Green	• Mean decrease in TSB per hour (umol/L/hour)	F20T12B) and 5 green fluorescent lamps (Sylvania F20T12G)
Romagnoli (1988) RCT	Preterm infants Mean age at PT = 57.5 hours Baseline mean TSB = 190.6 umol/L	Conventional PT-Blue vs Conventional PT-Green	• Mean decrease in TSB from baseline at 72 hours (in %)	Blue fluorescent (Philips TL/20W/03) and green fluorescent lamps (Sylvania F20T12G)
Positions				
Bhethanabhotla (2013) RCT	Term infants Mean age at PT = 87 hours Baseline mean TSB = Not reported	Conventional PT – Supine vs Conventional PT - Changing	• Mean duration of PT (hours) • Mean decrease in TSB per hour (umol/L/hour)	Changing: alternately supine or prone every 120 minutes
Chen (2002) RCT	Term infants Mean age at PT = 144 hours Baseline mean TSB = Not reported	Conventional PT – Supine vs Conventional PT - Changing	• Mean duration of PT (hours) • Mean decrease in TSB per hour (umol/L/hour) • Mean decrease in TSB from baseline at 24 hours (in %)	Changing: alternately supine or prone every 120 minutes
Donneborg (2010) RCT	Term infants Mean age at PT = Not reported Baseline mean TSB = Not reported	LED PT – Supine vs LED PT - Changing	• Mean decrease in TSB from baseline at 24 hours (in %)	Changing: infants were in supine position, then it was changed every third hour from supine to prone and vice versa.
Mohammadzadeh (2004) RCT	Term infants Mean age at PT = Not reported Baseline mean TSB = 321 umol/L	Conventional PT – Supine vs Conventional PT - Changing	• Mean decrease in TSB from baseline at 24 hours (umol/L)	Changing: alternately between supine and prone
Shinwell (2002)	Term infants	Conventional PT –	• Mean duration of PT (hours)	Changing: alternately supine or

Study reference (including study design)	Study population	Intervention & comparator	Outcomes reported	Comments
RCT	Mean age at PT = 103.5 hours Baseline mean TSB = 314.6 umol/L	Supine vs Conventional PT - Changing	• Mean decrease in TSB from baseline at 24 hours (umol/L) • Mean decrease in TSB from baseline at 24 hours (in %)	prone every 150 minutes
Curtains				
Babaei (2013) RCT	Term infants Mean age at PT = 144 hours Baseline mean TSB = 334.3 umol/L	Conventional PT vs Conventional PT + Curtains	• Mean duration of PT (hours) • Mean decrease in TSB from baseline at 12 hours (umol/L) • Mean decrease in TSB from baseline at 24 hours (umol/L) • Mean decrease in TSB from baseline at 36 hours (umol/L) • Mean decrease in TSB from baseline at 48 hours (umol/L)	Curtains: white shiny plastic curtains which covered three sides of the unit
Djokomuljanto (2006) RCT	Term infants Mean age at PT = 105 hours Baseline mean TSB = 263.8 umol/L	Conventional PT vs Conventional PT + Curtains	• Mean decrease in TSB from baseline at 4 hours (umol/L)	Curtains: white curtains were hung on both sides if the phototherapy unit.
Eggert (1988) RCT	Term infants Mean age at PT = 68.5 hours Baseline mean TSB = 245.3 umol/L	Conventional PT vs Conventional PT + Curtains	• Mean decrease in TSB from baseline at 24 hours (in %)	Curtains: white curtains - the four outer walls of the incubator were draped in white cloth.
Sivanandan (2009) RCT	Term infants Mean age at PT = 69 hours Baseline mean TSB = 279.5 umol/L	Conventional PT vs Conventional PT + Curtains	• Mean duration of PT (hours) • Mean decrease in TSB from baseline at 24 hours (in %) • Mean decrease in TSB from baseline at 4 hours (umol/L)	Curtains: the curtains were made up of white plastic sheets with reflecting inner surface, used to cover three sides of the unit.
Hamid (2013) RCT	Term infants	Double Conventional PT vs Conventional PT + Curtains	• Mean decrease in TSB from baseline at 4 hours (umol/L)	Curtains: the curtains were made using silver-coloured reflecting cloth, hanged and covered the

Study reference (including study design)	Study population	Intervention & comparator	Outcomes reported	Comments
	Mean age at PT = 131 hours Baseline mean TSB = 344 umol/L		• Mean decrease in TSB from baseline at 10 hours (umol/L) • Rebound jaundice	whole cot except for the foot end part. Double PT: 2 units of the conventional PT.
Intermittent phototherapy				
Lau (1984) RCT	Term infants Mean age at PT = Not reported Baseline mean TSB = 197.8 umol/L	Continuous Conventional PT vs Intermittent Conventional PT	• Mean duration of PT (hours) • Mean decrease in TSB per hour (umol/L/hour)	Intermittent Phototherapy: 4 hours on - 4 hours off (group 2) 1 hour on - 3 hours off (group 3)
Feedings				
Boo (2002) RCT	Term infants Mean age at PT = 139.2 hours Baseline mean TSB = 377.5 umol/L	Conventional PT + Enteral feeds vs Conventional PT + 50% Enteral feeds + 50% IV feeds	• Mean decrease in iSB per hour (umol/L/hour) • Exchange transfusion	Enteral: formula-fed babies were given 8 divided feeds at 3 hour intervals. Breastfed babies were breastfed on demand. IV: continuous intravenous 1/5 normal saline and 5% dextrose infusion
Martinez (1993) RCT	Term infants Mean age at PT = Not reported Baseline mean TSB = 307.5 umol/L	Conventional PT-Continue breastfeeding vs Conventional PT-Formula feeds	• Mean decrease in TSB from baseline at 48 hours (umol/L)	Not reported.
Mehta (2005) RCT	Term infants Mean age at PT = Not reported Baseline mean TSB = 349.5 umol/L	Conventional PT + Usual feeds vs Conventional PT + Usual feeds + Extra fluids	• Mean duration of PT (hours) • Mean decrease in TSB from baseline at 8 hours (in %) • Mean decrease in TSB from baseline at 24 hours (in %) • Exchange transfusion	Extra fluids consisted of IV fluid supplementation with N/5 saline in 5% dextrose for a period of 8 hours before PT.
Distance of phototherapy				
Vanborg (2012)	Term infants	LED PT at 47cm vs 38cm vs 29cm vs	• Mean decrease in TSB from	LED: neoBlue was used at

Study reference (including study design)	Study population	Intervention & comparator	Outcomes reported	Comments
RCT	Median age at PT = 81 hours Baseline mean TSB = 291.2 umol/L	20cm	baseline at 24 hours (umol/L) • Mean decrease in TSB from baseline at 24 hours (in %)	various distances.

1 *(a) Ayyash (1987a) – multi-arm trial*
2 *PT = phototherapy; TSB = total serum bilirubin.*

2.11 Health economic evidence review, review question 2

2.11.1 Methods

Evidence of cost effectiveness

The Committee is required to make decisions based on the best available evidence of both clinical and cost effectiveness. Guideline recommendations should be based on the expected costs of the different options in relation to their expected health benefits rather than the total implementation cost.

Evidence on cost effectiveness related to the key clinical issues being addressed in the guideline update was sought. The health economist undertook a systematic review of the published economic literature.

Economic literature search

A systematic literature search was undertaken to identify health economic evidence within published literature relevant to the review questions 1 and 2. The evidence was identified by conducting a broad search relating to phototherapy in the NHS Economic Evaluation Database (NHS EED) and the Health Technology Assessment database (HTA). The search also included Medline and Embase databases using an economic filter combined with the clinical search terms. Studies published in languages other than English were not reviewed. The search was conducted on 18 March 2015. The health economic search strategies are detailed in appendix J.

The health economist also sought out relevant studies identified by the surveillance review or Committee members.

Economic literature review

The health economist:

- Identified potentially relevant studies for each review question from the economic search results by reviewing titles and abstracts. Full papers were then obtained.
- Reviewed full papers against prespecified inclusion and exclusion criteria to identify relevant studies.

Inclusion and Exclusion criteria

Full economic evaluations (studies comparing costs and health consequences of alternative courses of action: cost-utility, cost-effectiveness, cost-benefit and cost-consequence analyses) and comparative costing studies that address the review question in the relevant population were considered potentially includable as economic evidence. Studies that only reported burden of disease or cost of illness were excluded. Literature reviews, abstracts, posters, letters, editorials, comment articles, unpublished studies and studies not in English were excluded.

Remaining studies were prioritised for inclusion based on their relative applicability to the development of this guideline and the study limitations. For example, if a high quality, directly applicable UK analysis was available, then other less relevant studies may not have been included. Where selective exclusions occurred on this basis, this is noted in the excluded economic studies table (appendix L).

For more details about the assessment of applicability and methodological quality see the economic evaluation checklist contained in *Appendix H* of *Developing NICE Guidelines: the manual 2014*.

Cost-effectiveness criteria

NICE's report *Social value judgements: principles for the development of NICE guidance* sets out the principles that GDGs should consider when judging whether an intervention offers good value for money. In general, an intervention was considered to be cost effective if either of the following criteria applied (given that the estimate was considered plausible):

- the intervention dominated other relevant strategies (that is, it was both less costly in terms of resource use and more clinically effective compared with all the other relevant alternative strategies), or
- the intervention cost less than £20,000 per QALY gained compared with the next best strategy.

If the Committee recommended an intervention that was estimated to cost more than £20,000 per QALY gained, or did not recommend one that was estimated to cost less than £20,000 per QALY gained, the reasons for this decision are discussed explicitly in the 'evidence to recommendations' section of the relevant chapter, with reference to issues regarding the plausibility of the estimate or to the factors set out in *Social value judgements: principles for the development of NICE guidance*.

In the absence of economic evidence

When no relevant economic studies were found from the economic literature review, and de novo modelling was not feasible or prioritised, the Committee made a qualitative judgement about cost-effectiveness by considering expected differences in resource use between options and relevant UK NHS unit costs, alongside the results of the clinical review of effectiveness evidence. The UK NHS costs reported in the guideline were those presented to the Committee and they were correct at the time recommendations were drafted; they may have been revised subsequently by the time of publication. However, we have no reason to believe they have been changed substantially.

2.11.2 Results of the economic literature review, review question 2

169 articles were identified by the initial combined search for review questions 1 and 2. 162 of these were excluded based on the title of the article and abstract. Seven articles were selected for consideration of the full version. Three of these could not be obtained and the other 4 were excluded. The flowchart summarising this review process can be found in appendix K. The list of excluded studies and the reasons for their exclusion can be found in appendix L.

2.12 Evidence statements

2.12.1 Clinical evidence statements

Colour of light bulbs/lamps

Conventional phototherapy

1 RCT (N = 141) suggested that preterm babies under conventional turquoise phototherapy had greater mean decrease in TSB from baseline after 24 hours compared to those under conventional blue phototherapy. (low quality)

4 RCTs (N = ranged from 30 to 83) provided inconclusive evidence on different outcomes between conventional blue phototherapy and conventional green phototherapy. Some suggested there was no clear evidence of a difference on mean duration of phototherapy between the 2 treatments for term babies but shorter duration for preterm babies under green phototherapy. Some evidence suggested babies under green phototherapy had better outcomes on mean decrease in TSB per hour and rebound jaundice while some evidence suggested babies under blue phototherapy had better outcomes on mean decrease in TSB from baseline after 24 and 72 hours. (low to very low quality)

LED phototherapy

1 small RCT (N = 47) on term babies suggested that there was no clear evidence of differences in mean duration of phototherapy and mean decrease in TSB between LED blue phototherapy and LED blue-green phototherapy. (low quality)

Positions for phototherapy

Conventional phototherapy

3 RCTs (N = ranged from 30 to 100) suggested that, during conventional phototherapy, there was no clear evidence of differences between term babies in supine positions compared to babies in alternate changing positions in mean duration of phototherapy and mean decrease in TSB. (moderate to very low quality)

LED phototherapy

1 RCT (N = 112) suggested that, during LED phototherapy, there was no clear evidence of a difference in mean decrease in TSB between term babies in supine position and those in alternate changing positions. (low quality)

Curtains for phototherapy

Conventional phototherapy

3 RCTs (N = ranged from 70 to 100) suggested that term babies under conventional phototherapy with curtains had a greater mean decrease in TSB compared to no curtains. 2 RCTs suggested there was no clear evidence of a difference between the 2 treatments for the mean duration of phototherapy and 1 RCT suggested there was no difference for skin rash and hyperthermia. (low to very low quality)

1 RCT (N = 156) on term babies suggested there was no clear evidence of differences in mean decrease in TSB and rebound jaundice between double conventional phototherapy and single conventional phototherapy with curtains. (moderate to low quality)

Feeds for phototherapy

Conventional phototherapy

1 RCT (N = 74) suggested that term babies under conventional phototherapy with normal feeds and extra fluids had a shorter mean duration of phototherapy, a greater mean decrease in TSB and fewer exchange transfusions, compared to babies receiving normal feeds without extra fluids (low quality). Another 2 RCTs (N = 54 and 74) suggested enteral feeds, IV feeds, formula feeds or breastfeeding had no significant impact on term babies' outcomes under conventional phototherapy (moderate to low quality).

Intermittent phototherapy

Conventional phototherapy

1 small RCT (N = 34) on term babies suggested that there was no clear evidence of differences in the mean duration of phototherapy and the mean decrease in TSB between continuous conventional phototherapy and intermittent conventional phototherapy for term babies. (very low quality)

No included studies reported purulent eye discharge, conjunctivitis, hydration and parental experience/acceptability as study outcomes.

2.12.28 Health economic evidence statements

No studies were identified by the economic literature review.

2.130 Evidence to recommendations

	Committee discussions
Relative value of different outcomes	The committee discussed the evidence and agreed that the three most important outcomes are the rate of decrease of serum bilirubin, adverse effects of phototherapy particularly transepidemal water loss or dehydration, and experiences of parents and staff. The committee acknowledged that no evidence identified reported experiences of parents and/or staff. The committee stated that this could be a very useful surrogate outcome for assessing how distressed or comfortable babies are when they are under phototherapy, as well as mother/baby interaction. With the same confounding factors of the actual spectrum and level of irradiance used in the phototherapy (as in review question1), the committee felt it was difficult to draw any conclusion by comparing all the reported outcomes. The committee in general felt that current evidence is unclear to suggest any differences on these outcomes.
Quality of evidence	The committee agreed that the majority of evidence was of low to very low quality due to study design issues (unclear randomisation methods and allocation concealment) and small sample size. These factors have increased their uncertainty in drawing any conclusion that there are differences between different procedures used to deliver phototherapy.
Trade-off between benefits and harms	The committee noted that in order to consider the trade off between benefits and harms of different procedures for delivering phototherapy, they would need clear evidence on which modality of phototherapy is the most effective first. As the committee was unable to draw conclusion on which modality of photothepy is the most effective, they felt they could not make any recommendation on the procedures of phototherapy because: • Almost all evidence on different procedures was from conventional phototherapy, and that there is uncertainty how this could be extrapolated to LED and fiberoptic phototherapy. • Most evidence was of low to very low quality. • The volume of evidence for different procedures was patchy and limited. • The uncertainty of the confounding factors of spectrum and irradiance, and how these interacted with different procedures in the studies. As a result, the committee felt that they could not draw any conclusion

	Committee discussions
	regarding what procedures are best for delivering phototherapy, and therefore they felt there was insufficient evidence to change any current recommendations.
Trade-off between net health benefits and resource use	No studies were identified that investigated the cost effectiveness of the methods of providing phototherapy. The Committee determined that different procuedures used to provide phototherapy would involve very minimal cost differences.
Other considerations	Overall, the committee agreed that, based on current evidence, they could not make any specific recommendation on procedures for delivering phototherapy. They agreed that existing recommendations on feeds, breaks and breastfeeding should stand.

2.14 Recommendations

Monitoring the baby during phototherapy

5. During phototherapy[a]:

- using clinical judgement, encourage short breaks (of up to 30 minutes) for breastfeeding, nappy changing and cuddles
- continue lactation/feeding support
- do not give additional fluids or feeds routinely.

Maternal expressed milk is the additional feed of choice if available, and when additional feeds are indicated. [2015]

6. During intensified phototherapy[b]:

- do not interrupt phototherapy for feeding but continue administering intravenous/enteral feeds
- continue lactation/feeding support so that breastfeeding can start again when treatment stops.

Maternal expressed milk is the additional feed of choice if available, and when additional feeds are indicated. [2015]

Definition:

[a] Phototherapy given using artificial light sources with appropriate spectrum and irradiance. This can be delivered by light-emitting diode (LED), fibreoptic or fluorescent lamps or tubes or bulbs.

[b] Phototherapy that is given with an increased level of irradiance with an appropriate spectrum. Phototherapy can be intensified by adding another light source or increasing the irradiance of the initial light source used.

2.15 Research recommendations

This area was not priorotised for further research.

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Holtrop PC, Ruedisueli K, Maisels MJ (1992) Double versus single phototherapy in low birth weight newborns. Pediatrics 90: 674-7.

Kumar P, Murki S, Malik GK et al. (2010) Light emitting diodes versus compact fluorescent tubes for phototherapy in neonatal jaundice: a multi center randomized controlled trial. Indian Pediatrics 47: 131-7.

Lau SP, Fung KP (1984) Serum bilirubin kinetics in intermittent phototherapy of physiological jaundice. Archives of Disease in Childhood 59: 892-4.

Martinez JC, Maisels MJ, Otheguy L et al. (1993) Hyperbilirubinemia in the breast-fed newborn: a controlled trial of four interventions. Pediatrics 91: 470-3.

Martins BM, de CM, Moreira ME et al. (2007) Efficacy of new microprocessed phototherapy system with five high intensity light emitting diodes (Super LED). Jornal de Pediatria 83: 253-8.

Mehta S, Kumar P, Narang A (2005) A randomized controlled trial of fluid supplementation in term neonates with severe hyperbilirubinemia. Journal of Pediatrics 147: 781-5.

Mohammadzadeh A, Bostani Z, Jafarnejad F et al. (2004) Supine versus turning position on bilirubin level during phototherapy in healthy term jaundiced neonates. Saudi Medical Journal 25: 2051-2.

Ngerncham S, Jirapaet K, Suvonachai R et al. (2012) Effectiveness of conventional phototherapy versus Super light-emitting diodes phototherapy in neonatal hyperbilirubinemia. Journal of the Medical Association of Thailand 95: 884-9.

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Romagnoli C, Marrocco G, Carolis MP et al. (1988) Phototherapy for hyperbilirubinemia in preterm infants: green vs blue or white light. Journal of Pediatrics 112: 476-81

Romagnoli C, Zecca E, Papacci P et al. (2006) Which phototherapy system is most effective in lowering serum bilirubin in very preterm infants? Fetal Diagnosis & Therapy 21: 204-9.

Sarici SU, Alpay F, Dundaroz MR et al. (2001) Fiberoptic phototherapy versus conventional daylight phototherapy for hyperbilirubinemia of term newborns. Turkish Journal of Pediatrics 43: 280-5.

Seidman DS, Moise J, Ergaz Z et al. (2000) A new blue light-emitting phototherapy device: a prospective randomized controlled study. Journal of Pediatrics 136: 771-4.

Seidman DS, Moise J, Ergaz Z et al. (2003) A prospective randomized controlled study of phototherapy using blue and blue-green light-emitting devices, and conventional halogen-quartz phototherapy. Journal of Perinatology 23: 123-7.

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Surmeli-Onay O, Korkmaz A, Yigit S et al. (2013) Phototherapy rash in newborn infants: does it differ between conventional and light emitting diode phototherapy? Pediatric Dermatology 30: 529-33.

Vandborg PK, Hansen BM, Greisen G et al. (2012) Dose-response relationship of phototherapy for hyperbilirubinemia. Pediatrics 130: e352-e357.

Vergunst-van Keulen JG et al. (1998) Fibre optic versus conventional phototherapy for hyperbilirubinaemia in preterm infants. European Journal of Pediatrics 157: 132-7.

Viau CJ, Rountree C, Destarac MA et al. (2012) Prospective randomized controlled study comparing low-cost LED and conventional phototherapy for treatment of neonatal hyperbilirubinemia. Journal of Tropical Pediatrics 58: 178-83.

4 Glossary and abbreviations

Please refer to the NICE glossary.

1 Appendices

2 Appendix A: Standing committee 3 members and NICE teams

A.1 4 Core members

Name	Role
Damien Longson (Chair)	Consultant Liaison Psychiatrist, Manchester Mental Health and Social Care Trust
Catherine Briggs	GP Principal, Bracondale Medical Centre, Stockport
John Cape	Director of Psychological Therapies Programme, University College London
Alun Davies	Professor of Vascular Surgery and Honorary Consultant Surgeon, Charing Cross & St Mary's Hospital & Imperial College NHS Trust
Alison Eastwood	Senior Research Fellow, Centre for Reviews and Dissemination, University of York
Sarah Fishburn	Lay Member
Jim Gray	Consultant Medical Microbiologist, The Birmingham Children's Hospital NHS Foundation Trust
Kath Nuttall	Director, Lancashire & South Cumbria Cancer Network (- April 2013)
Tilly Pillay	Consultant Neonatologist, Staffordshire, Shropshire and Black Country Newborn Network, Royal Wolverhampton Hospitals Trust
Nick Screaton	Radiologist, Papworth Hospital NHS Foundation Trust
Lindsay Smith	Principal in General Medical Practice, Somerset
Philippa Williams	Lay Member
Sophie Wilne	Paediatric Oncologist, Nottingham Children's Hospital

A.2 5 Topic expert Committee members

Name	Role
Chris Chaloner	Deputy Head of Service, Clinical Biochemistry
Jane Coyne	Community Midwife
Chris Edwards (non-voting expert)	Consultant Medical Physicist
Maria Jenkins	Lay member
Aung Soe	Consultant Neonatal Paediatrician
Julia Thomson	Paediatric Consultant

A.3 6 NICE project team

Name	Role
Mark Baker	Clinical Advisor
Christine Carson	Guideline Lead
Bhash Naidoo	Technical Lead (Health Economics)
Steven Barnes	Technical Lead
Louise Shires	Guideline Commissioning Manager
Joy Carvill	Guideline Co-ordinator (until June 2015)
Trudie Willingham	Guideline Co-ordinator (from June 2015)

Name	Role
Jessica Fielding	Public Involvement Advisor
Catharine Baden-Daintree	Editor

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A.42 Clinical guidelines update team

Name	Role
Philip Alderson	Clinical Advisor
Emma Banks	Co-ordinator
Jenny Craven	Information Specialist
Paul Crosland	Health Economist
Nicole Elliott	Associate Director
Nick Lowe	Administrator
Rebecca Parsons	Project Manager
Nitara Prasannan	Technical Analyst
Toni Tan	Technical Adviser

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1 Appendix B: Declarations of interest

2

Member name	Interest declared	Type of interest	Decision
Damien Longson	Family member employee of NICE.	Personal family non-specific	Declare and participate
Damien Longson	Director of Research & Innovation, Manchester Mental Health & Social Care NHS Trust.	Personal non-specific financial	Declare and participate
Catherine Briggs	Husband is a consultant anaesthetist at the University Hospital of South Manchester.	Personal family non-specific	Declare and participate
Catherine Briggs	Member of the Royal College of Surgeons, the Royal College of General Practitioners, the Faculty of Sexual and Reproductive Health and the BMA.	Personal non-specific financial	Declare and participate
Catherine Briggs	Chaired a discussion panel on urinary tract infections in women for Amco.	Personal non-specific financial	Declare and participate
John Cape	Trustee of the Anna Freud Centre, a child and family mental health charity which applies for and receives grants from the department of health and the national institute for health research.	Personal non-specific non-financial	Declare and participate
John Cape	Member of British Psychological Society & British Association for Behaviour & Cognitive Psychotherapists who seek to influence policy towards psychology & psychological therapies.	Personal non-specific non-financial	Declare and participate
John Cape	Clinical Services Lead half-day a week to Big Health, a digital health company that has one commercial product; an online CBT self-help programme for insomnia with online support	Personal non-specific financial	Declare and participate
Alun Davies	Research grant funding – commercial: Vascular Insights; Acergy Ltd; Firstkind; URGO laboratoire; Sapheon Inc (terminated 2013). All administered by Imperial	Personal non-specific financial	Declare and participate

Member name	Interest declared	Type of interest	Decision
	College London as Sponsor and Professor Davies as CI.		
Alun Davies	Research grant funding – non-commercial: National Institute for Health Research, British Heart Foundation, Royal College of Surgeons, Circulation Foundation, European Venous Forum.	Personal non-specific financial	Declare and participate
Alun Davies	Non-commercial: Attendance at numerous national & international meetings as an invited guest to lecture where the organising groups receive funding from numerous sources including device and pharmaceutical manufacturers. Organising groups pay expenses and occasionally honoraria - the exact source of funding is often not known.	Personal non-specific financial	Declare and participate
Alison Eastwood	Member of an independent academic team at Centre for Review & Dissemination, University of York commissioned by NICE through NIHR to undertake technology assessment reviews.	Non-personal non-specific financial	Declare and participate
Sarah Fishburn	Organises workshops for physiotherapists treating pelvic girdle pain. Paid for this work.	Personal non-specific financial	Declare and participate
Sarah Fishburn	Payment and expenses from the Nursing and Midwifery Council as a lay panellist of the Fitness to Practise Investigating Committee.	Personal non-specific financial	Declare and participate
Sarah Fishburn	Lay reviewer with the Local Supervising Authority auditing supervision of midwives - payment and expenses for this work.	Personal non-specific financial	Declare and participate
Sarah Fishburn	Lay reviewer for the National Institute for Health Research; has reviewed a number of research proposals being considered for funding.	Personal non-specific financial	Declare and participate

Member name	Interest declared	Type of interest	Decision
	Paid for carrying out these reviews.		
Sarah Fishburn	Chair of the Pelvic Partnership, a support group for women with pregnancy-related pelvic girdle pain (voluntary position).	Personal non-specific financial	Declare and participate
Sarah Fishburn	Trained as a chartered physiotherapist and qualified in 1988 but have not been in clinical practice since 1997. Remains a non-practicing member of the Chartered Society of Physiotherapy.	Personal non-specific financial	Declare and participate
Sarah Fishburn	Appointed by Mott MacDonald to carry out reviews as a lay reviewer on behalf to the Nursing and Midwifery Council of Local Supervising Authorities and Universities providing courses for nurses and midwives. This is paid work.	Personal non-specific financial	Declare and participate
Jim Gray	Deputy Editor, Journal of Hospital Infection, funded by the Healthcare Infection Society (HIS pay the hospital for my time)	Personal financial non-specific	Declare and participate
Jim Gray	Co-investigator in four major trials (3 HTA-funded; 1 British Council funded. Two trials are about antibiotic prophylaxis on obstetrics and gynaecology to prevent pelvic infections, one is comparing different suture materials and the fourth is a diagnostic test accuracy study for use in woman in labour).	Non-personal financial non-specific	Declare and participate
Jim Gray	Associate Editor, International Journal of Antimicrobial Agents.	Non-personal financial non-specific	Declare and participate
Jim Gray	Associate Editor Journal of Pediatric Infectious Diseases.	Non-personal financial non-specific	Declare and participate
Jim Gray	Expert Advisor, British National Formulary for Children.	Non-personal financial non-specific	Declare and participate
Jim Gray	My Department is in receipt of an Educational Grant from Pfizer Ltd to	Non-personal financial non-specific	Declare and participate

Member name	Interest declared	Type of interest	Decision
	develop improved diagnosis of invasive fungal infections in immunocompromised children		
Jim Gray	Small shareholding (under £2000) in Glaxo Smith Kline	Personal financial	Declare and participate
Kath Nuttall	None		Declare and participate
Tilly Pillay	None		Declare and participate
Nick Screaton	Attended Thorax meeting – travel expenses paid.	Non-specific personal financial	Declare and participate
Nick Screaton	Clinical Commissioning Group stakeholder member	Non-specific personal non-financial	Declare and participate
Nick Screaton	Senior Editor British Journal of Radiology	Non-specific personal non-financial	Declare and participate
Nick Screaton	Advisory Editor Clinical Radiology	Non-specific personal non-financial	Declare and participate
Nick Screaton	Chair East of England British Institute of Radiology	Non-specific personal non-financial	Declare and participate
Nick Screaton	Director – Cambridge Clinical Imaging LTD	Non-specific personal financial	Declare and participate
Nick Screaton	British Thoracic Society Bronchiectasis Guidelines Group	Non-specific personal non-financial	Declare and participate
Nick Screaton	Specialised Imaging Clinical Commissioning Group stakeholder member	Non-specific personal non-financial	Declare and participate
Nick Screaton	Member of the Faculty Board for the Royal College of Radiologists	Non-specific personal non-financial	Declare and participate
Nick Screaton	Member of the Editorial Board of Pulmonary Circulation	Non-specific personal non-financial	Declare and participate
Lindsay Smith	None		Declare and participate
Philippa Williams	None		Declare and participate
Sophie Wilne	Recipient of NHS Innovation Challenge Award for clinical awareness campaign to reduce delays in diagnosis of brain tumours in children & young adults. Award will be used to develop the campaign.	Personal non-specific non-financial	Declare and participate
Sophie Wilne	Co-investigator for RFPB grant to undertake systematic reviews in childhood brain tumours.	Personal non-specific non-financial	Declare and participate
Sophie Wilne	Co-investigator for grant	Personal non-specific non-	Declare and participate

Member name	Interest declared	Type of interest	Decision
	awards from charity to evaluate impact of brain tumour awareness campaign.	financial	
Sophie Wilne	Funding for travel and accommodation from Novartis to attend a conference on the management of tuberous sclerosis	Personal non-specific financial	Declare and participate
Topic expert	**Interest declared**	**Type of interest**	**Decision**
Christopher Chaloner	None		Declare and participate
Julia Thomson	None		Declare and participate
Jane Coyne	None		Declare and participate
Maria Jenkins	None		Declare and participate
Aung Soe	None		Declare and participate
Chris Edwards	None		Declare and participate

1 Appendix C: Review protocol

C.1 2 Review question 1

	Details
Review question 1	What is the best modality of giving phototherapy (clinical and cost-effectiveness)?
Background/Objectives	Phototherapy is considered to be an effective method of treating jaundice in neonates. However, there is doubt on the best modality of giving phototherapy with clinical feedback suggesting that LED phototherapy is now more effective than the older light source types. The aim of this review therefore is to evaluate the best modality of giving phototherapy.
Original review questions (if relevant)	What is the best modality of giving phototherapy (clinical and cost-effectiveness)? a) conventional phototherapy (single, double or multiple phototherapy) b) sunlight c) fibreoptic phototherapy (biliblankets, bilibeds and other products)
Type of review question	Intervention
Language	English language only
Study design	Systematic reviews of RCT, randomised controlled trials
Status	Published studies (full text only)
Population	Newborns with a diagnosis of jaundice (but otherwise well) Subgroups: preterm babies versus term babies
Intervention	Conventional phototherapy (single, double or multiple phototherapy)
Comparator	a) sunlight* b) fibreoptic phototherapy (biliblankets, bilibeds and other products)* c)LED phototherapy (LED spot lights) d) LED phototherapy (LED pads) *Data on any comparisons (as opposed to specific pair-wise comparisons) should be analysed
Outcomes	<u>Important outcomes</u> 1) Number of exchange transfusions 2) Treatment failure (as defined in the study) including cases of rebound jaundice and kernicterus 3) Mean duration of phototherapy 4) Staff experience 5) Adverse events of phototherapy including mortality <u>Critical outcomes</u> 1) Mean change in serum bilirubin and rate of decline of bilirubin 2) Parental experience/acceptability including access for bonding and breastfeeding
Other criteria for inclusion / exclusion of studies	Exclude: - studies looking at the effect of phototherapy in combination with other treatments or prophylaxis studies
Review strategies	*A list of excluded studies will be provided following sifting of the database *Data on all included studies will be extracted into evidence tables *Where statistically possible, a meta-analytical approach will be used

	to give an overall summary effect *For intervention question, all critical and important outcomes from evidence will be presented in GRADE profiles (where appropriate) and further summarized in evidence statements.

C.21 Review question 2

	Details
Review question 2	What is the correct procedure of giving phototherapy?
Background/Objectives	The recommendations concerning the modality of phototherapy are out of date in terms of current clinical practice as LEDs are already the dominant form of phototherapy. Any new evidence that utilises LED phototherapy may impact guidance if this type of phototherapy is additionally recommended in any update of this guideline. Therefore, this review aimed to evaluate the correct procedure of giving phototherapy. We will be examining the correct procedure for all modes of phototherapy rather than the most effective modality (as determined by question 1) as although some modes may be more effective than others, the ease/difficulty of procedures involved in each mode as well as the cost-effectiveness of various modes would also need to be considered before recommending a particular mode of phototherapy.
Original review questions (if relevant)	What is the correct procedure when administering phototherapy (with specific reference to method of feeding/types of feed, incubator or bassinet care, the effect of intermittent versus constant phototherapy on maternal-infant bonding, and parental anxiety)?
Type of review question	Intervention
Language	English language only
Study design	Systematic reviews of RCTs, randomised controlled trials
Status	Published studies (full text only)
Population	Newborns with a diagnosis of jaundice (but otherwise well) Subgroups: preterm babies versus term babies
Intervention	1) Fixed position 2) Eye coverings 3) Intermittent feeds (brief interruptions of phototherapy treatment to facilitate breastfeeding and cuddles) 4) Curtains 5) Incubators/bassinets 6) Bulb colour 7) Size of fibreoptic pads (small vs large) 8) Light intensity/distance of phototherapy device
Comparator	1) Changing position* 2) No/other types of eye coverings * 3) Continuous feeds/breast/bottle/nasogastric tube feeding* 4) No curtains* 5) No incubators/bassinets* 6) Different bulb colour 7) Different sized pad 8) Different light intensity/distance of phototherapy device *Data on any comparisons (as opposed to specific pair-wise comparisons) should be analysed
Outcomes	Important outcomes

	1) Mean duration of treatment 2) Cases of purulent eye discharge 3) Features of conjunctivitis 4) Hydration 5) Adverse events of phototherapy including mortality <u>Critical outcomes</u> 1) Mean change in serum bilirubin and rate of decline of bilirubin 2) Parental experience/acceptability including access for bonding and breastfeeding
Other criteria for inclusion / exclusion of studies	None
Review strategies	*A list of excluded studies will be provided following sifting of the database *Data on all included studies will be extracted into evidence tables *Where statistically possible, a meta-analytical approach will be used to give an overall summary effect *For intervention question, all critical and important outcomes from evidence will be presented in GRADE profiles (where appropriate) and further summarized in evidence statements.

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Appendix D: Search strategy

Databases that were searched, together with the number of articles retrieved from each database for each question are shown in table 16 and 17.

D.1 Review question 1 and 2

Table 4: Clinical search summary (review question 1 and 2)

Databases	Date searched	No. retrieved
CDSR (Ovid, Wiley)	11/02/2015	15
Database of Abstracts of Reviews of Effects – DARE (CRD, Ovid, Wiley)	11/02/2015	5
HTA database (CRD, Ovid, Wiley)	11/02/2015	4
CENTRAL (Ovid, Wiley)	11/02/2015	349
MEDLINE (Ovid)	11/02/2015	446
MEDLINE In-Process (Ovid)	11/02/2015	20
EMBASE (Ovid)	11/02/2015	441

Table 5: Clinical search terms (review question 1 and 2)

Line number/Search term/Number retrieved
Ovid MEDLINE
1 exp Infant, Newborn/ (500668)
2 (newborn* or neonat* or preterm* or premature*).tw. (378958)
3 1 or 2 (694268)
4 Hyperbilirubinemia/ (3894)
5 exp Jaundice/ (11843)
6 Kernicterus/ (1034)
7 (bilirubin* or hyperbilirubin* or jaundice* or kernicterus* or icterus*).tw. (53866)
8 (bilirubin adj2 encephalopath*).tw. (352)
9 or/4-8 (59492)
10 Jaundice, Neonatal/ (5321)
11 Hyperbilirubinemia, Neonatal/ (564)
12 10 or 11 (5809)
13 3 and 9 (11108)
14 12 or 13 (12504)
15 exp Phototherapy/ (28537)
16 (phototherap* or heliotherap* or sunlight or actinotherap*).tw. (13359)

17	Fiber Optic Technology/ (13219)
18	(photoradiati* adj4 therap*).tw. (181)
19	((light or fibre or ultraviolet) adj4 (therap* or technolog*)).tw. (3959)
20	(biliblanket* or bilibed* or bilisoft*).tw. (19)
21	(bilirubin adj4 (blanket* or pad*)).tw. (1)
22	(wallaby or wallabies).tw. (1130)
23	(optic adj2 fibre*).tw. (1307)
24	(light adj1 emitting adj1 diode*).tw. (2881)
25	(LED adj4 light*).tw. (1808)
26	((fluorescen* or halogen*) adj4 (light* or lamp*)).tw. (7377)
27	(vickers adj4 flourescent*).tw. (0)
28	"mediprema cradle*".tw. (0)
29	neoblue*.tw. (3)
30	((micro-lite or micro lite) adj4 phototherapy*).tw. (0)
31	ohmeda*.tw. (421)
32	medela*.tw. (19)
33	medestime*.tw. (0)
34	draeger*.tw. (178)
35	(hill-rom* or hill rom*).tw. (35)
36	or/15-35 (65123)
37	14 and 36 (2025)
38	animals/ not human/ (3889478)
39	37 not 38 (2003)
40	limit 39 to english language (1603)
41	Meta-Analysis.pt. (52487)
42	Meta-Analysis as Topic/ (13933)
43	Review.pt. (1913954)
44	exp Review Literature as Topic/ (7810)
45	(metaanaly$ or metanaly$ or (meta adj3 analy$)).tw. (62102)
46	(review$ or overview$).ti. (273471)
47	(systematic$ adj5 (review$ or overview$)).tw. (57312)
48	((quantitative$ or qualitative$) adj5 (review$ or overview$)).tw. (4410)
49	((studies or trial$) adj2 (review$ or overview$)).tw. (25150)
50	(integrat$ adj3 (research or review$ or literature)).tw. (5518)

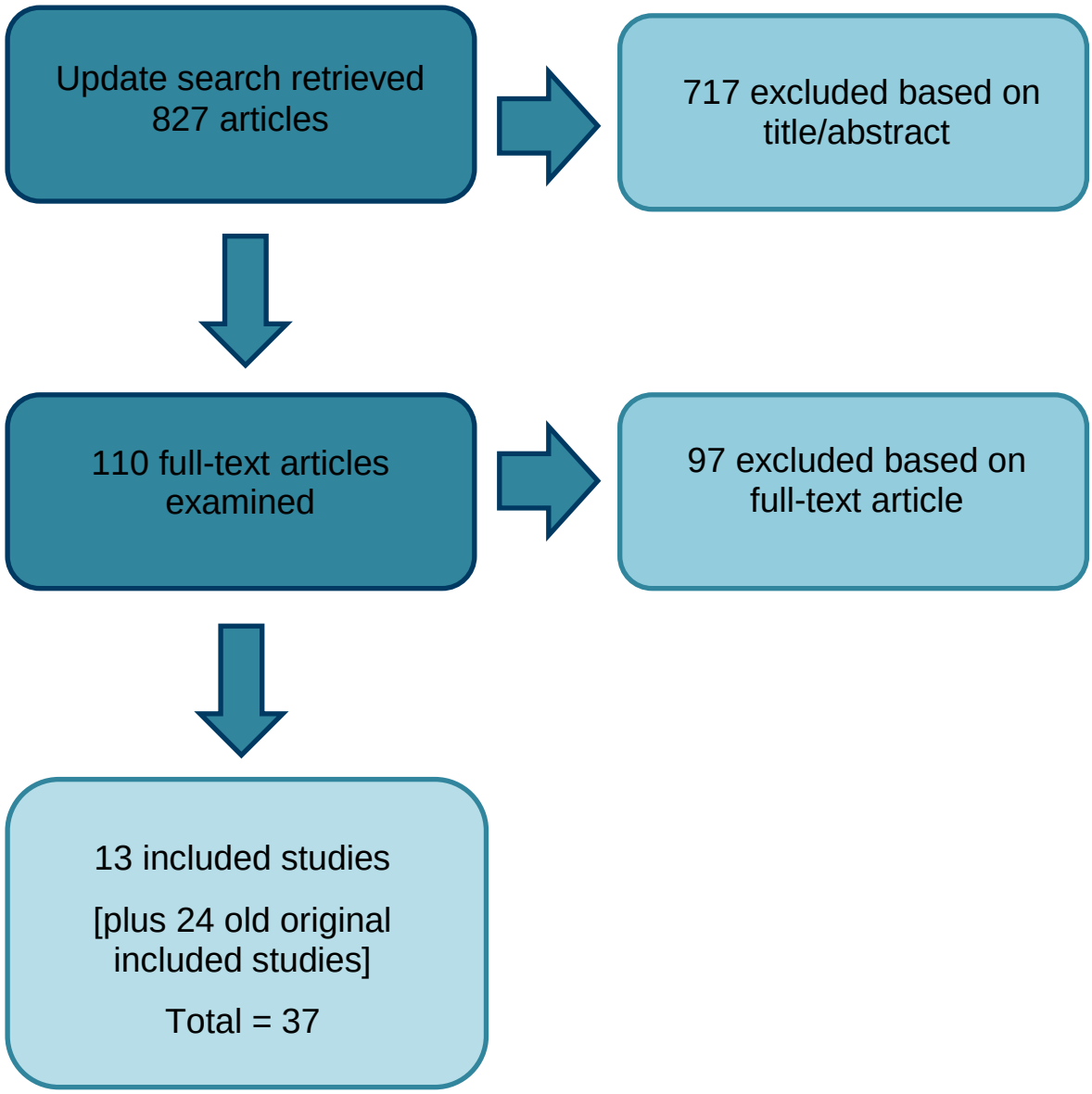
51	(pool$ adj2 (analy$ or data)).tw. (14251)
52	(handsearch$ or (hand adj3 search$)).tw. (5346)
53	(manual$ adj3 search$).tw. (3161)
54	or/41-53 (2075650)
55	14 and 54 (1261)
56	animals/ not humans/ (3889478)
57	54 not 56 (1940472)
58	Randomized Controlled Trial.pt. (383316)
59	Controlled Clinical Trial.pt. (88500)
60	Clinical Trial.pt. (488432)
61	exp Clinical Trials as Topic/ (283986)
62	Placebos/ (32521)
63	Random Allocation/ (81900)
64	Double-Blind Method/ (127355)
65	Single-Blind Method/ (19790)
66	Cross-Over Studies/ (35008)
67	((random$ or control$ or clinical$) adj3 (trial$ or stud$)).tw. (745110)
68	(random$ adj3 allocat$).tw. (20962)
69	placebo$.tw. (153173)
70	((singl$ or doubl$ or trebl$ or tripl$) adj (blind$ or mask$)).tw. (125002)
71	(crossover$ or (cross adj over$)).tw. (57114)
72	or/58-71 (1392469)
73	animals/ not humans/ (3889478)
74	72 not 73 (1297513)
75	57 or 74 (2997589)
76	40 and 75 (446)

1

Appendix E: Review flowchart

E.1 Review question 1 and 2

Update search for question 1 and 2 were conducted under one search



1 Appendix F:Excluded studies

F.12 Review question 1 and 2

Reference	Reason for exclusion
Anon (1985) Randomized, controlled trial of phototherapy for neonatal hyperbilirubinemia. Executive summary. Pediatrics 75: t-6.	Summary of an old included study.
Amato M, Howald H, Muralt G (1985) Interruption of breast-feeding versus phototherapy as treatment of hyperbilirubinemia in full-term infants. Helvetica Paediatrica Acta 40: 127-31.	Not all babies received phototherapy.
Amato M, Feller CH, Huppi P (1992) Conventional versus fiberoptic phototherapy for treatment of neonatal hyperbilirubinemia. Dev Physiopat Clin 3: 61.	BL unable to supply
Argent AC, Rothberg AD, Cooper PA (1984) Effect of phototherapy (Px) at 3 bilirubin (bili) thresholds in term neonates with physiologic hyperbilirubinemia (H B). Pediatric Research 18: 344.	Abstract only, insufficient data for appraisal.
Arnold C, Pedroza C, Tyson JE (2014) Phototherapy in ELBW newborns: does it work? Is it safe? The evidence from randomized clinical trials. Seminars in Perinatology 38: 452-64.	Narrative review.
Ashok KD, ET AL (2008) A Multi-Centre Randomized Controlled Trial of Light-Emitting Diodes (LED) Versus Compact Fluorescent Tubes (CFT) for Phototherapy in Neonatal Jaundice. Pediatric Academic Society http://www.abstracts2view.com/pas/	BL unable to supply
Bhethanabhotla S, Deorari A, Paul V et al. (2013) Effect of Infant Position during Phototherapy in Management of Hyperbilirubinemia in Late Preterm and Term Neonates: RCT. Pediatric Academic Societies Annual Meeting	Abstract on an included study.
Boo NY, Lee HT (2002) Randomized controlled trial of oral versus intravenous fluid supplementation on serum bilirubin level during phototherapy of term infants with severe hyperbilirubinaemia. [Erratum appears in J Paediatr Child Health 2002 Dec;38(6):625]. Journal of Paediatrics & Child Health 38: 151-5.	Intervention and comparator not as specified in protocol.
Boo NY, Chew EL (2006) A randomised control trial of clingfilm for prevention of hypothermia in term infants during phototherapy. Singapore Medical Journal 47: 757-62.	Intervention (clingfilm) not in the review protocol.
Broughton PM, Rossiter EJ, Warren CB et al. (1965) Effect of blue light on hyperbilirubinaemia. Archives of Disease in Childhood 40: 666-71.	Intervention and comparator not as specified in protocol.
Bryla DA (1985) Randomized, controlled trial of phototherapy for neonatal hyperbilirubinemia. Development, design, and sample composition. Pediatrics 75: t-92.	Only the research protocol.
Chang YS, Hwang JH, Kwon HN et al. (2005) In vitro and in vivo efficacy of new blue light emitting diode phototherapy compared to conventional halogen quartz phototherapy for neonatal jaundice. Journal of Korean medical science 20: 61-4.	Animal study.
Deorari AK, Kumar P, Murki S et al. (2009) A Multi-Centre Randomized Controlled Trial of Light-Emitting Diodes (LED) Versus Compact Fluorescent Tubes (CFT) for Phototherapy in Neonatal Jaundice. Pediatric Academic Societies Annual Meeting; 2009 May 2 5; Baltimore MD, United States	Abstract only, insufficient data for appraisal.
Dijk PH, Hulzebos CV (2012) An evidence-based view on hyperbilirubinaemia. Acta Paediatrica, International Journal of Paediatrics.101 (SUPPL.464) (pp 3-10), 2012.Date of Publication: April 2012. 3-10.	Narrative review

Reference	Reason for exclusion
Donzelli GP, Moroni M, Paparo M et al. (1992) Phototherapy for neonatal jaundice: a comparative study of fiber optic light and fluorescent lamps. Pediatric Research 32: 625A.	Abstract only, insufficient data for appraisal.
Donzelli GP, Moroni M, Pratesi S et al. (1996) Fibreoptic phototherapy in the management of jaundice in low birthweight neonates. Acta Paediatrica 85: 366-70.	Not an RCT – sequentially enrolled patients to each group – cohort study.
Ebbesen F (2005) Therapeutic Effect of Turquoise Light Versus Blue in Preterm Infants with Jaundice. Pediatric Academic Societies Annual Meeting; 2005 May 14-17; Washington DC, United States	BL unable to supply
Ebbesen FO, Agati G (2002) Phototherapy with turquoise versus special blue light in preterm infants with jaundice. Pediatric Research 51: 343A.	Abstract only, insufficient data for appraisal.
Edris AA, Ghany EA, Razek AR et al. (2014) The role of intensive phototherapy in decreasing the need for exchange transfusion in neonatal jaundice. JPMA - Journal of the Pakistan Medical Association 64: 5-8.	Not an RCT.
Eggert P, Hoft S, Stick C (1995) Frequent turning of jaundiced neonates during phototherapy. A simple means of increasing efficacy. Padiatrische Praxis 50: 201-6.	Not in English.
Ek-isariyaphorn R, Maneenut R, Kardreunkaew J et al. (2013) The efficacy of the in-house light-emitting diode phototherapy equipment compare to conventional phototherapy equipment on the treatment of neonatal hyperbilirubinemia. Journal of the Medical Association of Thailand 96: 1536-41.	BL unable to supply
Elliott E, Moncrieff MW, George WHS (1974) Phototherapy for hyperbilirubinaemia in low birthweight infants. Archives of Disease in Childhood 49: 60-2.	Not an RCT and not all babies received phototherapy.
Ennever JF, Knox I, Speck WT (1986) Differences in bilirubin isomer composition in infants treated with green and white light phototherapy. Journal of Pediatrics 109: 119-22.	Study design unclear, not an RCT.
Evans D (2007) Neonatal jaundice. Clinical Evidence 2007, 2007.	Narrative review.
Fakhraee SH, Kazemian M, Afjeh SA et al. (2011) Effect of infants' position during phototherapy on the level of serum bilirubin. Journal of Isfahan Medical School.29 (153) (pp 1169-1175), 2011.Date of Publication: November 2011. 1169-75.	Not in English
French S (2003) Phototherapy in the home for jaundiced neonates (Structured abstract). Health Technology Assessment Database : 15.	BL unable to supply
Garg AK, Prasad RS, Hifzi IA (1995) A controlled trial of high-intensity double-surface phototherapy on a fluid bed versus conventional phototherapy in neonatal jaundice. Pediatrics 95: 914-6.	Not an RCT.
George P, Lynch M (1994) Ohmeda Biliblanket vs Wallaby Phototherapy System for the reduction of bilirubin levels in the home-care setting. Clinical Pediatrics 33: 178-80.	Comparator not in the review protocol (fiberoptic vs. fiberoptic).
HAYES, Inc (2007) Phototherapy blankets versus standard phototherapy lights for the treatment of neonatal hyperbilirubinemia (Structured abstract). Health Technology Assessment Database	BL unable to supply
Hysmith T, Hysmith S, Farmer D (1992) A comparison of fiberoptic vs overhead fluorescent bank methods of phototherapy for the home-care-appropriate preterm infant. Journal of Perinatology 12: 91	Abstract only, insufficient data for appraisal.
Iranpour R, Mohammadizadeh M, Nazem-Sadati S (2011) Comparison of two phototherapy Methods (prophylactic vs therapeutic) for management of hyperbilirubinemia in very low birth weight newborns. Iranian Journal of Pediatrics 21: 425-30.	Study looks at when to start phototherapy (within hours of birth versus serum bilirubin trigger) - this is outside the scope of this update.

Reference	Reason for exclusion
Jangaard KA, Vincer MJ, Allen AC (2007) A randomized trial of aggressive versus conservative phototherapy for hyperbilirubinemia in infants weighing less than 1500 g: Short- and long-term outcomes. Paediatrics and Child Health.12 (10) (pp 853-858), 2007.Date of Publication: December 2007. 853-8.	Study looks at when to start phototherapy (within hours of birth versus serum bilirubin trigger) - this is outside the scope of this update.
Jodeiry B, Fakhraee S-H, Kazemian M et al. (2013) Rebound hyperbilirubinaemia in neonates admitted to Mofid Children's Hospital, Tehran, Iran. SAJCH South African Journal of Child Health.7 (1) (pp 22-24), 2013.Date of Publication: 2013. 22-4.	Not an RCT.
Kale Y, Aydemir O, Celik U et al. (2013) Effects of phototherapy using different light sources on oxidant and antioxidant status of neonates with jaundice. Intensive Care Medicine.Conference: 24th Annual Meeting of the European Society of Paediatric and Neonatal Intensive Care, ESPNIC 2013 Rotterdam Netherlands.Conference Start: 20130612 Conference End: 20130615.Conference Publication: (var.pagings).39 (: S15-S16.	Abstract only, insufficient data for appraisal.
Kang JH, Shankaran S (1992) Double phototherapy with high irradiance compared with standard phototherapy. Pediatric Research 31: 207A.	Abstract only, insufficient data for appraisal.
Kang JH, Shankaran S (1995) Double phototherapy with high irradiance compared with single phototherapy in neonates with hyperbilirubinemia. American Journal of Perinatology 12: 178-80.	Not an RCT.
Karadag A, Yesilyurt A, Unal S et al. (2009) A chromosomal-effect study of intensive phototherapy versus conventional phototherapy in newborns with jaundice. Mutation Research 676: 17-20.	Not relevant – genetic study.
Kargar M, Jamshidi Z, Beheshtipour N et al. (2014) Effect of head covering on phototherapy-induced hypocalcaemia in icterus newborns; a randomized controlled trial. International Journal of Community Based Nursing & Midwifery 2: 121-6.	Intervention not as specified in the review protocol.
Kato S, Kakita H, Yamada Y et al. (2014) Cycrobilirubin formation capacity as a novel index in phototherapy for neonatal hyperbilirubinemia in a randomised controlled study. Archives of Disease in Childhood.Conference: 5th Congress of the European Academy of Paediatric Societies, EAPS 2014 Barcelona Spain.Conference Start: 20141017 Conference End: 20141021.Conference Publication: (var.pagings).99 (pp A460), 2014.Date of : A460.	Abstract only, insufficient data for appraisal.
Khorana M, Lamloetviriyakit P, Apornviriyawongse P (2012) Outcomes of two different interventions in term neonates with breast milk jaundice. Breastfeeding Medicine.Conference: 17th Annual International Meeting of the Academy of Breastfeeding Medicine Chicago, IL United States.Conference Start: 20121011 Conference End: 20121014.Conference Publication: (var.pagings).7 (pp S3-S4), 2012.Date : S3-S4.	Abstract only, insufficient data for appraisal.
Krueger Jr RC, Hanna L, Bockenhauer S et al. (2001) An unblinded, prospective, randomized trial comparing two methods of phototherapy for neonatal jaundice: efficacy and parental satisfaction. Pediatric Research 49: 324A.	Abstract only, insufficient data for appraisal.
Kumar P, Chawla D, Deorari A (2009) Light-emitting diode phototherapy for unconjugated hyperbilirubinemia in neonates. Cochrane Database of Systematic Reviews .	Protocol only.
Kumar P, Chawla D, Deorari A (2011) Light-emitting diode phototherapy for unconjugated hyperbilirubinaemia in neonates. [Review]. Cochrane Database of Systematic Reviews : CD007969.	Cochrane review does not assess all outcomes specified by the topic experts: therefore individual

Reference	Reason for exclusion
	studies within this review have been reviewed separately. Used as cross checking.
Kurt A, Aygun AD, Kurt AN et al. (2009) Use of phototherapy for neonatal hyperbilirubinemia affects cytokine production and lymphocyte subsets. Neonatology 95: 262-6.	Not an RCT and no relevant outcomes.
Ludington-Hoe SM, Swinth JY (2001) Kangaroo mother care during phototherapy: effect on bilirubin profile. Neonatal Network - Journal of Neonatal Nursing 20: 41-8.	Not relevant - Comparison of three methods of giving 24 hour phototherapy.
Maisels MJ, Kring EA, DeRidder J (2007) Randomized controlled trial of light-emitting diode phototherapy. Journal of Perinatology 27: 565-7.	New recruited patients and readmitted patients groups were merged in the outcomes where the interventions and comparators were slightly different.
Maisels MJ, Watchko JF, Bhutani VK et al. (2012) An approach to the management of hyperbilirubinemia in the preterm infant less than 35 weeks of gestation. [Review]. Journal of Perinatology 32: 660-4.	Narrative review.
Mali PH (2004) Nurse's responsibilities in phototherapy. [Review] [5 refs]. Nursing Journal of India 95: 19-20.	Narrative review.
Martinez JC, Maisels MJ, Otheguy L et al. (1992) Management of severe hyperbilirubinemia in fullterm newborns-a controlled trial of 4 interventions. Pediatric Research 31: 211A.	BL unable to supply
Martins B, Carvalho M (2010) Light-Emitting Diodes versus Compact Fluorescent Tubes for Phototherapy. Indian Pediatrics 47: 979.	Commentary only, not primary RCT.
Maurer HM, Kirkpatrick BV, McWilliams NB et al. (1985) Phototherapy for hyperbilirubinemia of hemolytic disease of the newborn. Pediatrics 75: 407-12.	Unclear comparator.
Mehta S, Kumar P, Narang A (2005) A randomized controlled trial of fluid supplementation in term neonates with severe hyperbilirubinemia. Journal of Pediatrics 147: 781-5.	Intervention not as specified in the review protocol.
Meritano J, Nieto R, Solana C et al. (2012) Efficacy of conventional blue light lamps vs.. LED phototherapy with two levels of irradiance. Pediatric Research.Conference: 49th Annual Meeting of the Latin American Society for Pediatric Research, LASPR 2011 Guanajuato Mexico.Conference Start: 20111106 Conference End: 20111109.Conference Publication: (var.pagings).72 (1) (pp 109), 2012.Date : 109.	Abstract only, insufficient data for appraisal.
Mills JF, Tudehope D (2001) Fibreoptic phototherapy for neonatal jaundice. [Review] [47 refs]. Cochrane Database of Systematic Reviews : CD002060.	2001 Cochrane review – only used for cross checking individual studies for inclusion.
Mohammadizadeh M, Eliadarani FK, Badiei Z (2012) Is the light-emitting diode a better light source than fluorescent tube for phototherapy of neonatal jaundice in preterm infants? Advanced Biomedical Research 1: 51.	Not an RCT – alternate allocation – cohort study.
Myara A, Sender A, Valette V et al. (1997) Early changes in cutaneous bilirubin and serum bilirubin isomers during intensive phototherapy of jaundiced neonates with blue and green light. Biology of the Neonate 71: 75-82.	N<5 each arm, outcomes unclear.
Naderi S, Safdarian F, Mazloomi D et al. (2009) Efficacy of double and triple phototherapy in term newborns with hyperbilirubinemia: the first clinical trial. Pediatrics & Neonatology 50: 266-9.	Comparators not in the review protocol (double vs triple conventional PT).

Reference	Reason for exclusion
Niknafs P, Mortazavi A-A, Torabinejad MH et al. (2008) Intermittent versus continuous phototherapy for reducing neonatal hyperbilirubinemia. Iranian Journal of Pediatrics.18 (3) (pp 251-256), 2008.Date of Publication: September 2008. 251-6.	Not relevant - study compares 2 forms of intermittent phototherapy
Okwundu CI, Okoromah CAN, Shah PS (2009) Prophylactic phototherapy for preventing jaundice in preterm very low birth weight infants. Cochrane Database of Systematic Reviews	Not relevant – about prophylaxis.
Okwundu CI, Okoromah CA, Shah PS (2012) Prophylactic phototherapy for preventing jaundice in preterm or low birth weight infants. [Review]. Cochrane Database of Systematic Reviews 1: CD007966.	Cochrane review focuses on timing of phototherapy initiation - before bilirubin has reached a pre-specified level versus therapy starting when bilirubin has reached a certain level: this is outside of the scope of this update.
Okwundu CI, Okoromah CA, Shah PS (2013) Prophylactic phototherapy for preventing jaundice in preterm or low birth weight infants (Structured abstract). Evidence-Based Child Health 8: 204-49.	Abstract of a Cochrane review that has been requested.
Olah J, Toth-Molnar E, Kemeny L et al. (2013) Long-term hazards of neonatal blue-light phototherapy. [Review]. British Journal of Dermatology 169: 243-9.	Narrative review
Onyango AB, Suresh G, Were F (2009) Intermittent phototherapy versus continuous phototherapy for neonatal jaundice. Cochrane Database of Systematic Reviews	Only protocol for Cochrane review
Outerbridge EW, Beaudry MA, Chance GW (1986) Use of phototherapy for neonatal hyperbilirubinemia. Canadian Medical Association Journal.134 (11) (pp 1237-1245), 1986.Date of Publication: 1986. 1237-45.	Narrative review
Pritchard MA, Beller EM, Norton B (2004) Skin exposure during conventional phototherapy in preterm infants: A randomized controlled trial. Journal of Paediatrics & Child Health 40: 270-4.	Comparators not in review protocol - comparison of 2 combinations of positioning combined with clothing.
Rodgers N, Yuille G, Guillet R et al. (2013) Phototherapy in Moderately Preterm Neonates with Non-Hemolytic Hyperbilirubinemia: Indications for Discontinuation. Pediatric Academic Societies Annual Meeting	BL unable to supply
Romagnoli C, Polidori G (1976) Growth of preterm babies during and after phototherapy. <ORIGINAL> ACCRESCIMENTO PONDERALE IN NEONATI PRETERMINE DURANTE E DOPO FOTOTERAPIA. RIVITALPEDIAT 2: 323-8.	BL unable to supply
Romagnoli C, Frezza S, Greco F et al. (1994) Phototherapic treatment of the hyperbilirubinemia of the full-term neonate: Fiberoptic or conventional systems? Aggiornamento pediatrico 45: 61-7.	Not in English.
Romagnoli C, Frezza S, Menonna NM et al. (1995) Fiberoptic phototherapy or conventional phototherapy in the treatment of neonatal hyperbilirubinemia. Rivista italiana di pediatria [Italian journal of pediatrics] 21: 198-205.	Not in English.
Rosenfeld W, Twist P, Concepcion L (1990) A new device for phototherapy treatment of jaundiced infants. Journal of Perinatology 10: 243-8.	Study not an RCT - subjects were allocated to groups based on preference of physician and agreement of parents.
Sachdeva M, Murki S, Oleti TP et al. (2014) Intermittent versus continuous phototherapy for the treatment of neonatal non-hemolytic	Methodology flaw – it's an interim report where the

Reference	Reason for exclusion
moderate hyperbilirubinemia in infants more than 34 weeks of gestational age: a randomized controlled trial. European Journal of Pediatrics	trial stopped early as positive results were identified. (duplicate)
Sachdeva M, Murki S, Oleti TP et al. (2015) Intermittent versus continuous phototherapy for the treatment of neonatal non-hemolytic moderate hyperbilirubinemia in infants more than 34 weeks of gestational age: a randomized controlled trial. European Journal of Pediatrics 174: 177-81.	Methodology flaw – it's an interim report where the trial stopped early as positive results were identified.
Sadeghnia A, Ganji M, Armanian AM (2014) A comparison between the effect of fluorescent lamps and quartz halogen incandescent filament lamps on the treatment of hyperbilirobinemia in newborns with the gestational age of 35 weeks or more. International Journal of Preventive Medicine.5 (9) (pp 1186-1191), 2014.Date of Publication: 01 Sep 2014. 1186-91.	No extractable data, unclear how TSB was reported with different denominators.
Saeidi R, Heydarian F, Fakehi V (2009) Role of intravenous extra fluid therapy in icteric neonates receiving phototherapy. Saudi Medical Journal 30: 1176-9.	Intervention not as specified in protocol.
Saeidi R, Heydarian F, Fakehi V et al. (2009) Role of intravenous extra fluid therapy in icteric neonates receiving phototherapy Early nasal intermittent positive pressure ventilation versus continuous positive airway pressure for respiratory distress syndrome. Saudi Medical Journal 30: 1176-9.	Not relevant.
Sarici SU, Alpay F, Unay B et al. (1999) Comparison of the efficacy of conventional special blue light phototherapy and fiberoptic phototherapy in the management of neonatal hyperbilirubinaemia. Acta Paediatrica 88: 1249-53.	Not an RCT.
Sarici SU, Alpay F, Unay B et al. (2000) Double versus single phototherapy in term newborns with significant hyperbilirubinemia. Journal of Tropical Pediatrics 46: 36-9.	Not an RCT.
Sarin M, Dutta S, Narang A (2006) Randomized controlled trial of compact fluorescent lamp versus standard phototherapy for the treatment of neonatal hyperbilirubinemia. Indian Pediatrics 43: 583-90.	Comparison not in the review protocol (type of blue burb).
Schuman AJ, Karush G (1992) Fiberoptic vs conventional home phototherapy for neonatal hyperbilirubinemia. Clinical Pediatrics 31: 345-52.	Study not an RCT, treatment group was based on availability of phototherapy and preference of the clinician.
Sharma SK, Sood SC, Sharma A et al. (1985) Double versus single surface phototherapy in neonatal hyperbilirubinemia. Indian Pediatrics 22: 235-9.	Not an RCT.
Shoemaker MD, Ellis MR, Meadows S (2003) Should jaundiced infants be breastfed? Journal of Family Practice.52 (11) (pp 895-896), 2003.Date of Publication: November 2003. 895-6.	Narrative review
Silva I, Luco M, Tapia JL et al. (2009) Single vs. double phototherapy in the treatment of full-term newborns with nonhemolytic hyperbilirubinemia. Jornal de Pediatria 85: 455-8.	Not in English.
Slusher TM, Olusanya BO, Vreman HJ et al. (2013) Treatment of neonatal jaundice with filtered sunlight in Nigerian neonates: study protocol of a non-inferiority, randomized controlled trial. Trials [Electronic Resource] 14: 446.	Only a research protocol for an ongoing trial.
Srivastava KL, Misra PK, Kaul R et al. (1980) Double surface phototherapy versus single surface phototherapy in neonatal jaundice. Indian Journal of Medical Research 71: 746-50.	Study design unclear, not an RCT.
Tabb PA, Savage DC, Inglis J et al. (1972) Controlled trial of phototherapy of limited duration in the treatment of physiological	Intervention and comparator not as specified

Reference	Reason for exclusion
hyperbilirubinaemia in low-birth-weight infants. Lancet 2: 1211-2.	in protocol; study examines groups of different durations of phototherapy.
Tan KL, Chow MT, Karim SMM (1977) The nature of the dose response relationship of phototherapy for neonatal hyperbilirubinemia. Journal of Pediatrics 90: 448-2.	Study design unclear, not an RCT.
Tan KL (1994) Comparison of the efficacy of fiberoptic and conventional phototherapy for neonatal hyperbilirubinemia. Journal of Pediatrics 125: 607-12.	Not an RCT – no randomisation.
Tayman C, Tatli MM, Aydemir S et al. (2010) Overhead is superior to underneath light-emitting diode phototherapy in the treatment of neonatal jaundice: a comparative study. Journal of Paediatrics & Child Health 46: 234-7.	Not an RCT – clinical team decided which treatment to allocate rather than randomisation.
Thaithumyanon P, Visutiratmanee C (2002) Double phototherapy in jaundiced term infants with hemolysis. Journal of the Medical Association of Thailand 85: 1176-81.	Study not an RCT - participants were divided into groups based on the availability of the phototherapy bed.
Thitiratsanont N, Chamnanvanakij S (2013) Efficacy of a Local Made Phototherapy Device Using Light-Emitting Diodes (LED) Lamps for Treatment of Neonatal Hyperbilirubinemia. Pediatric Academic Societies Annual Meeting	Abstract only, insufficient data for appraisal.
Tridente A, De LD (2012) Efficacy of light-emitting diode versus other light sources for treatment of neonatal hyperbilirubinemia: a systematic review and meta-analysis. [Review]. Acta Paediatrica 101: 458-65.	Systematic review does not assess the same outcomes specified by the topic experts - individual studies included in this review have therefore been reviewed separately. Used as cross-checking.
Tyson JE, Pedroza C, Langer J et al. (2012) Does aggressive phototherapy increase mortality while decreasing profound impairment among the smallest and sickest newborns? Journal of Perinatology 32: 677-84.	Intervention and comparator not as specified in the review protocol.
Uras N, Karadag A, Tonbul A et al. (2009) Comparison of light emitting diode phototherapy and double standard conventional phototherapy for nonhemolytic neonatal hyperbilirubinemia. Turkish Journal of Medical Sciences 39: 337-41.	Study design unclear, not an RCT.
Woodall D, Karas JG (1992) A new light on jaundice A pilot study. Clinical Pediatrics 31: 353-6.	Not relevant – about home therapy and N<10 per arm.
Woodgate P, Jardine LA (2011) Neonatal jaundice. Clinical Evidence 2011, 2011.	2010 review article, used to cross check individual studies for inclusion.
Xiong T, Qu Y, Cambier S et al. (2011) The side effects of phototherapy for neonatal jaundice: what do we know? What should we do?. [Review]. European Journal of Pediatrics 170: 1247-55.	Narrative review.
Zainab K, Adlina S (2004) Effectiveness of home versus hospital phototherapy for term infants with uncomplicated hyperbilirubinemia: a pilot study in Pahang, Malaysia. Medical Journal of Malaysia 59: 395-401.	Not an RCT – matched cohort study.

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2

1 Appendix G: Evidence tables

G.1 2 Review question 1

Bibliographic reference **Q1: Old**	**Author: Holtrop P** **Double versus single phototherapy in low birth weight newborns.** **Year: 1992** **ID: 151**
Study type	RCT
Aim	To compare double with single phototherapy in low birth weight newborns
Patient characteristics	Inclusion: Birthweight < 2500, Birthweight between 10th and 90th percentile, > 24 1 day old, no congenital anomalies, no Rh incompatibility, TSB > 85 micromol/litre at BW < 1000gms, TSB > 103 micromol/litre at BW 1000 - 1200gms, TSB > 120 micromol/litre at BW 1200 - 1400gms, TSB > 137 micromol/litre at BW 1400 - 1600gms, TSB > 1071 micromol/litre at BW 1600 - 1800gms, TSB > 12 at BW 1800 - 2200gms, TSB 12 - 15 at BW 2200 - 2500gms Exclusion: Not reported
Number of Patients	N = 70 (conventional = 37, conventional + fibreoptic = 33) Demographics: Gender (male/female): conventional = 19/18, conventional+fibreoptic = 16/17 Gestational age (weeks, mean & SD): conventional = 30.2 (2.6), conventional+fibreoptic = 30.6 (2.9) Birth weight (g, mean & SD): conventional = 1533 (419), conventional+fibreoptic = 1502 (424) Age phototherapy started (hour, mean & SD): conventional = 58 (26), conventional+fibreoptic = 58 (26)
Intervention	Group 1: Conventional phototherapy Single Conventional phototherapy consisted of either 1/ if baby was in an incubator, a standard unit (Olympic Bili-lite) with 4 white and 4 blue fluorescent lamps 35 cm above the baby. Irradiance at skin level was 9.2microW/cm2/nm Light range was 425 – 475 Or 2/ if baby was on a radiant warmer, 3 halogen lights on each side(Air Shields7850) with an irradiance of 7microW/cm2/nm

Bibliographic reference **Q1: Old**	**Author: Holtrop P** **Double versus single phototherapy in low birth weight newborns.** **Year: 1992** **ID: 151**
	Babies wore eye patches and wore disposable diapers cut to allow maximum skin exposure Fluids were administered on clinician advice
Comparison	Group 2: Double phototherapy (Conventional phototherapy + Fiberoptic phototherapy) Double phototherapy consisted of single Conventional phototherapy as above combined with a 'Wallaby' fiberoptic blanket measuring 10 X 35 cm. Mean irradiance on the blanket's surface was 8.2microW/cm2/nm. Babies wore eye patches and wore disposable diapers cut to allow maximum skin exposure Fluids were administered on clinician advice
Length of follow up	One week after cessation of phototherapy
Location	USA
Outcomes measures and effect size	Mean decrease in TSB after 18 hours of phototherapy (in %, with SD): Conventional = 16% (15), conventional + fibreoptic = 31% (11) Mean decrease in TSB after 18 hours of phototherapy (in mg/dL, with SD): Conventional = 1.6 (1.4), conventional + fibreoptic = 2.9 (1.1) Rebound jaundice: Conventional = 14/37; conventional + fibreoptic = 12/33
Source of funding	Not reported.
Comments	Blinding: Not reported Randomisation: Computer generated. Randomisation was stratified by birth weight.

1

Bibliographic reference **Q1: Old**	**Author: Sarici S** **Fibreoptic phototherapy versus conventional daylight phototherapy for hyperbilirubinemia of term newborns.** **Year: 2001** **ID: 139**
Study type	RCT
Aim	To compare efficacy Fibreoptic phototherapy with conventional daylight phototherapy

Bibliographic reference **Q1: Old**	**Author: Sarici S** **Fibreoptic phototherapy versus conventional daylight phototherapy for hyperbilirubinemia of term newborns.** **Year: 2001** **ID: 139**
Patient characteristics	Inclusion: Birthweight > 2500 gms, Nonhemolytic indirect hyperbilirubinaemia, Normal Reticulocyte count, Negative DAT, No evidence of blood group isoimmunisation, TSB ≥ 256 micromol/litre. Phototherapy was initiated ar serum bilirubin levels of ≥15mg/dL. Exclusion: Direct hyperbilirubinaemia, Enclosed haemorrhage, Infection, congenital malformations
Number of Patients	N = 100 (conventional = 50; fibreoptic = 50) Demographics: Gender (M/F): conventional = 28/22, fibreoptic = 26/24 Mean GA (weeks with SD): conventional = 39.2 (0.67), fibreoptic = 38.9 (0.7) Mean BW (g, with SD): conventional = 3410 (300), fibreoptic = 3350 (410) Mean age at entry to study (h, with SD): conventional = 104.8 (41.3), fibreoptic = 106.0 (44.7) Mean TSB at start (mg/dL, with SD): conventional = 18.2 (2.8), fibreoptic = 17.8 (2.7)
Intervention	Group 1: Conventional phototherapy Conventional Phototherapy (Ohio Medical Products) consisted of a bank of 5 daylight fluorescent lamps 30cm above the baby
Comparison	Group 2: Fiberoptic phototherapy Fiberoptic phototherapy (Walley II Phototherapy System) consisted of a single pad (7.6 X 35.5 cm) Babies in both groups were placed in a prone position and all babies wore disposable diapers. Babies in the phototherapy group wore eye patches Irradiance and light range were not reported Phototherapy considered to have failure if two consecutive measures showed an increase in TSB
Length of follow up	Not reported.
Location	Turkey
Outcomes measures and effect size	Mean duration: Group 1: 49.4 ± 14.4 hours; Group 2: 61.0 ± 13.1 hours, p<0.05

Bibliographic reference **Q1: Old**	**Author: Sarici S** **Fibreoptic phototherapy versus conventional daylight phototherapy for hyperbilirubinemia of term newborns.** **Year: 2001** **ID: 139**
	Mean decrease in TSB (in %/hour, with SD): Group 1: -0.8%per hour (0.3); Group 2: -0.6% per hour (0.3), p<0.05 Rebound jaundice: Group 1: 3/50; Group 2: 2/50 Treatment failure (needing double phototherapy): Group 1: 0/50; Group 2: 4/50 Erythema: Group 1: 1/50; Group 2: 1/50 Watery stools: Group 1: 3/50; Group 2: 3/50
Source of funding	Not reported.
Comments	Blinding: Blind allocation Randomisation: Sequential allocated, no random component

1

Bibliographic reference **Q1: Old**	**Author: Gale R** **A randomised, controlled application of the Wallaby phototherapy system compared with standard phototherapy.** **Year: 1990** **ID: 140**
Study type	RCT
Aim	To compare the efficacy and feasibility of the Wallaby phototherapy system with standard phototherapy.
Patient characteristics	Inclusion: Full-term (> 37 weeks), No haemolytic jaundice, TSB > 200 micromol/litre but if babies had rapidly increasing TSB levels they could be entered into the study before they reached 200 micromol/litre. Exclusion: Evidence of hemolysis
Number of Patients	N = 42 (conventional = 22, fibreoptic = 20)

Bibliographic reference **Q1: Old**	**Author: Gale R** **A randomised, controlled application of the Wallaby phototherapy system compared with standard phototherapy.** **Year: 1990** **ID: 140**
	Demographics: Gender (M/F): Not reported Mean GA (weeks, mean & SD): conventional = 39.3 (1.9), fibreoptic = 39.3 (1.3) Mean BW (g, mean & SD): conventional = 3113 (398), fibreoptic = 3291 (542) Age at entry to study: Not reported Mean TSB at baseline (umol/L, mean & SD): conventional = 189.0 (88.1), fibreoptic = 184.5 (85.8)
Intervention	Group 1: Conventional phototherapy Conventional Phototherapy (Air Shields PT 53–3) consisted of a standard phototherapy unit (both daylight and blue lamps) positioned above the baby. Babies were naked, with eyes covered, and were alternate between prone and supine position every 6 hours. Irradiance at blanket level was 7.0 ± 0.5microW/cm2/nm.
Comparison	Group 2: Fiberoptic phototherapy Fiberoptic phototherapy (Wallaby Phototherapy System) consisted of a single fiberoptic pad linked to a lightbox with 150-watt halogen lamp and a fan with 150.ft2/minute air volume. Irradiance spectrum was between 425 and 475 nm. Irradiance at blanket level was 7.0 ± 0.5microW/cm2/nm. Babies were placed naked on the blanked. While nursing the mother could hold the baby wrapped in the blanket In both group babies were kept on phototherapy for 48 hours but could be withdrawn at any stage.
Length of follow up	Not reported
Location	USA
Outcomes measures and effect size	Mean decrease in TSB at 48 hours of phototherapy (umol/L, with SD): Conventional = -26.0 (46.0), fibreoptic = -24.3 (15.0), p>0.05 Number of infants ceased phototherapy at 48 hours (no longer required treatment): Conventional = 6/22, fibreoptic = 3/20
Source of funding	Not reported

Bibliographic reference **Q1: Old**	**Author: Gale R** **A randomised, controlled application of the Wallaby phototherapy system compared with standard phototherapy.** **Year: 1990** **ID: 140**
Comments	Blinding: Not reported Randomisation: Not reported, only stated randomly assigned.

1

Bibliographic reference **Q1: Old**	**Author: Dani C** **Effects of phototherapy on cerebral haemodynamics in preterm infants: is fibre-optic different from conventional phototherapy?** **Year: 2004** **ID: 153**
Study type	RCT
Aim	To test the hypothesis in a prospective study in which the cerebral haemodynamics of preterm infants who were randomized to receive CPT or FPT for hyperbilirubinemia were studied using cerebral Doppler ultrasonography.
Patient characteristics	Inclusion: Preterm (GA < 34 weeks), No haemolytic jaundice, not on respiratory support, Clinically stable. Exclusion: Major congenital malformations, patent ductus arteriosus, intracranial haemorrhage, Perinatal asphyxia, receiving cardiovascular drugs
Number of Patients	N = 23 (conventional = 12; fiberoptic = 11) Demographics: Gender (M/F): Not reported Mean GA (week, SD): conventional = 30.8 (1.5); fiberoptic = 31.3 (2.1) Mean BW (g, SD): conventional = 1430 (420); fiberoptic = 1509 (392) Mean age at entry to study (hour, SD): conventional = 67 (18); fiberoptic = 59 (10.2) Mean TSB at start of phototherapy (umol/L, SD): conventional =237 (8.6); fiberoptic = 247 (7.2)
Intervention	Group 1: Conventional phototherapy Conventional Phototherapy consisted of a Photo-Therapie 800 system. Baby was naked except for eye patches and in a supine position. Irradiance and light range not reported

Bibliographic reference **Q1: Old**	**Author: Dani C** **Effects of phototherapy on cerebral haemodynamics in preterm infants: is fibre-optic different from conventional phototherapy?** **Year: 2004** **ID: 153**
Comparison	Group 2: Fiberoptic phototherapy Fiberoptic phototherapy (BiliBlanket) consisted of a mat that covered the baby up to the upper abdomen. Irradiance and light range not reported To avoid trans-epidermal water loss the babies were placed in incubators with a thermo-monitoring system to maintain normal body temperature (46.5oC) at a relative humidity of 60%.
Length of follow up	Not reported.
Location	Italy
Outcomes measures and effect size	Mean duration of phototherapy (hour, SD): Group 1 = 43.0 ± 3.1 hours; Group 2 = 38.7 ± 4.5 hours Mean skin temperature 24-36 hours after the start of phototherapy (degree Celsius, SD): Group 1 = 36.4 (0.3); Group 2 = 36.6 (0.3)
Source of funding	Not reported.
Comments	Blinding: Not reported Randomisation: Allocation method not reported but sealed envelopes used

1

Bibliographic reference **Q1: Old**	**Author: Holtrop P** **A Clinical Trial of Fiberoptic Phototherapy vs Conventional Phototherapy** **Year: 1992** **ID: 141** **NOTE: NO USABLE OOUTCOME DATA**
Study type	RCT
Aim	To compare fiberoptic phototherapy with conventional phototherapy in healthy jaundiced newborns with birth weights greater than 2500 g.
Patient characteristics	Inclusion: Birthweight > 2500 gms, Age > 1 day, No Rh incompatibility, Clinical need for phototherapy

Bibliographic reference **Q1: Old**	**Author: Holtrop P** **A Clinical Trial of Fiberoptic Phototherapy vs Conventional Phototherapy** **Year: 1992** **ID: 141** **NOTE: NO USABLE OOUTCOME DATA**
	Exclusion: Not reported
Number of Patients	N = 26 (conventional = 14, fibreoptic = 12) Demographics: Gender (M/F): conventional = 8/6; fibreoptic = 9/3 Mean GA (SD): conventional = 37.6 wks (2.9); fibreoptic = 38.7 wks (1.9) Mean BW (SD): conventional = 3255g (525); fibreoptic = 3520g (547) Age at entry to study (h, mean & SD): conventional = 62.5 hrs (21); fibreoptic = 66.5 hrs (18) Mean TSB (baseline) (mean umol/L & SD): conventional = 231 (29); fibreoptic = 231 (21)
Intervention	Group 1: Conventional phototherapy Conventional phototherapy (Olympic Bili-lite) consisted of an overhead bank of 4 white and 4 blue 35 cm above the baby. Babies were naked except for diapers and eye patches. Babies were removed for feeding. Mean irradiance was 9.2 ± 0.9microW/cm2/nm
Comparison	Group 2: Fiberoptic phototherapy Fiberoptic phototherapy (Wallaby Phototherapy System) consisted of a cummerbund which was wrapped around the torso. Babies wore eye patches. Mean irradiance was 8.2 ± 1.2microW/cm2/nm Babies were removed from the study if the TSB rose by more than 9 micromol/litre/h
Length of follow up	Not reported
Location	USA
Outcomes measures and effect size	Mean TSB at 18 hrs of phototherapy (umol/L, mean & SD): Group 1 = 210 (24); Group 2 = 188 (26), p=0.035 Side effects (rashes, temperature):

Bibliographic reference **Q1: Old**	**Author: Holtrop P** **A Clinical Trial of Fiberoptic Phototherapy vs Conventional Phototherapy** **Year: 1992** **ID: 141** **NOTE: NO USABLE OOUTCOME DATA**
	Group 1: 0/14; Group 2: 0/12
Source of funding	Not reported
Comments	Blinding: Not reported Randomisation: Computer generated At 18 hours of treatment, two newborns in the fiberoptic group were changed to conventional phototherapy; one at the parents' request and one because the light bulb failed in the fiberoptic phototherapy system.

1

Bibliographic reference **Q1: Old**	**Author: Pezzati M** **Changes in skin temperature of hyperbilirubinemic newborns under pthtotherapy: conventional versus fibreoptic device.** **Year: 2002** **ID: 142**
Study type	RCT
Aim	To determine the changes in skin temperature.
Patient characteristics	Inclusion: Hyperbilirubinemic but otherwiaw healthy term infants, with appropriate size for gestational age. Exclusion: Not reported.
Number of Patients	N = 41 (conventional = 21, fiberoptic = 20) Demographics: Gender (M/F) : Not reported Mean GA (week, SD): conventional =39.6 (1.5), fiberoptic = 39.6 (1.7) Mean BW (g, SD): conventional = 3249 (349), fiberoptic = 3222 (364) Mean age at entry to study: Not reported Mean TSB at start of phototherapy (mg/dL, SD): conventional = 17.4 (1.49), fiberoptic = 17.1 (2.19)
Intervention	Group 1: Conventional Phototherapy

Bibliographic reference **Q1: Old**	**Author: Pezzati M** **Changes in skin temperature of hyperbilirubinemic newborns under pthtotherapy: conventional versus fibreoptic device.** **Year: 2002** **ID: 142**
	Conventional phototherapy ('Photo-Therapie 800') consisted of a unit incorporating a metal vapour discharge blue lamp with 2 filters (an infrared filter and a Plexiglas ultraviolet filter). A fan was fitted to remove heat generated by lamp.
Comparison	Group 2: Fiberoptic Phototherapy Fiberoptic phototherapy (BiliBlanket PT) consisted of a 140W quartz halogen lamp with a built-in dichroic reflector with low infrared and ultraviolet radiation reflectivity. Light range was restricted to 400 – 550 nm. All babies were naked in a supine position at a stabilised room temperature.
Length of follow up	Not reported
Location	Italy
Outcomes measures and effect size	Adverse effect: Mean skin temperature during phototherapy (degree Celsius, SD): Forehead: conventional =36.74 (0.7), fiberoptic = 36.27 (0.4) Abdomen: conventional =36.99 (0.6), fiberoptic = 36.52 (0.4) Left leg: conventional =36.41 (0.8), fiberoptic = 36.38 (0.3) Back: conventional =36.70 (0.6), fiberoptic = 36.62 (0.4)
Source of funding	Not reported
Comments	Blinding: Not reported Randomisation: Not report but sealed envelopes used

1

Bibliographic reference **Q1: Old**	**Author: Romagnoli C** **Which Phototherapy System Is Most Effective in Lowering Serum Bilirubin in Very Preterm Infants?** **Year: 2006** **ID: 152**
Study type	RCT
Aim	To compare the effectiveness of various phototherapy systems in lowering serum bilirubin levels in preterm infants.
Patient characteristics	Inclusion: TSB> 103 micromol/litre; GA < 30 weeks

Bibliographic reference **Q1: Old**	**Author: Romagnoli C** **Which Phototherapy System Is Most Effective in Lowering Serum Bilirubin in Very Preterm Infants?** **Year: 2006** **ID: 152**
	Exclusion: Infants with hemolytic anemia, congenital malformation, congenital infections, and neonates whose mothers had received phenobarbital.
Number of Patients	N = 136 (Group 1 = 33, Group 2 = 35, Group 3 = 35, Group 4 = 33) Demographics: Gender (M/F): Group 1 = 19/14, Group 2 = 18/17, Group 3 = 17/18, Group 4 = 18/15 Mean GA (weeks, SD): Group 1 = 27.9 (1.3), Group 2 = 27.9 (1.4), Group 3 = 27.9 (1.5), Group 4 = 28.0 (1.4) Mean BW (g, SD): Group 1 = 1000 (294), Group 2 = 1050 (309), Group 3 = 1014 (283), Group 4 = 1010 (251) Mean age at entry to study (hour, SD): Group 1 = 38.1 (7.2), Group 2 = 37.8 (7.4), Group 3 = 39.0 (6.9), Group 4 = 38.5 (7.2) Mean TSB (baseline (umol/L, SD): Group 1 = 109.4 (5.1), Group 2 = 109.4 (5.1), Group 3 = 112.2 (5.1), Group 4 = 107.7 (3.4)
Intervention	Group 1: Conventional phototherapy Conventional phototherapy consisted of standard phototherapy composed of 4 fluorescent lamps and 4 blue lamps 40cm above the baby. Irradiance at skin level was 22 – 24 microW/cm2/nm. Babies were naked except for eye patches and disposable diapers. Baby position was changed from prone to supine and vice versa every 6 hours.
Comparison	Group 2: Fiberoptic (Wallaby) phototherapy Group 3: Fiberoptic (BiliBlanket) phototherapy Group 4: Combined conventional and Fiberoptic (Wallaby) phototherapy Fiberoptic Wallaby phototherapy consisted of a 10.1 X 15.2 cm pad linked to a 150W quartz halogen lamp. A light filter is placed between the lamp and the fiberoptic bundle to allow only 400 – 550 nm range through. Irradiance at skin level was 8 – 10 microW/cm2/nm. Baby position was changed from prone to supine and vice versa every 6 hours. Fiberoptic BiliBlanket phototherapy consisted of an 11 X 13 cm pad linked to a 150W tungsten halogen lamp. A light filter is placed between the lamp and the fiberoptic bundle to allow only 400 – 550 nm range through. Irradiance at skin level was 35microW/cm2/nm. Baby position was changed from prone to supine and vice versa every 6 hours. Combined phototherapy consisted of conventional phototherapy as above and the fiberoptic Wallaby system as above.
Length of follow up	Not reported.

Bibliographic reference **Q1: Old**	**Author: Romagnoli C** **Which Phototherapy System Is Most Effective in Lowering Serum Bilirubin in Very Preterm Infants?** **Year: 2006** **ID: 152**
Location	Italy
Outcomes measures and effect size	No. of exchange transfusion: Group 1: 2/33; Group 2: 2/35; Group 3: 1/35; Group 4: 0/33 Erythema: Group 1: 10/33; Group 2: 9/35; Group 3: 8/35; Group 4: 12/33 Change in TSB concentration at 48-72hrs from baseline (in %, with SD): Group 1 = -5.1% (5.4); Group 2 = -2.8% (9.4); Group 3 = -5.6% (8.3); Group 4 = -13.5% (8.3) *p < 0.001 group 4 vs. 1, 2 and 3* Mean duration of phototherapy Group 1: 90.2 ± 24.3 hours; Group 2: 92.1 ± 43.3 hours; Group 3: 94.4 ± 43.3 hours; Group 4: 75.1 ± 23.6 hours Max TSB:: Group 1: 157 ± 43 micromol/litre; Group 2: 169 ± 56 micromol/litre; Group 3: 161 ± 44 micromol/litre; Group 4: 130 ± 22 micromol/litre
Source of funding	Not reported.
Comments	Blinding: Not reported Randomisation: Not reported but sealed envelopes used

1

Bibliographic reference **Q1: Old**	**Author: Van Kaam A** **Fibre optic versus conventional phototherapy for hyperbilirubinaemia in preterm infants** **Year: 1998** **ID: 154**
Study type	RCT
Aim	To compares efficacy of fibreoptic phototherapy using the Ohmeda Biliblanket device to conventional fluorescent phototherapy in preterm infants.
Patient	Inclusion:

Bibliographic reference **Q1: Old**	**Author: Van Kaam A** **Fibre optic versus conventional phototherapy for hyperbilirubinaemia in preterm infants** **Year: 1998** **ID: 154**
characteristics	Preterm babies with birthweight < 2000gms, Non-haemolytic jaundice Exclusion: Prior phototherapy, met criteria for exchange transfusion
Number of Patients	N = 124 (conventional = 68, fibreoptic = 56) Demographics: Gender (M/F) : 72/52 Mean GA: 29.7 ± 2.4 weeks Mean BW: 1250 ± 353 gms Age at entry to study: 26.5 ± 17.5 Mean TSB: 94 ± 36 micromol/litre
Intervention	Group 1: Conventional phototherapy Conventional phototherapy consisted of 4 overhead fluorescent lamps arranged in an arc 40 cm above the baby. Baby was naked except for eye patches. The light range is in the 380 – 480 nm range. Irradiance level was 16 microW/cm2/nm.
Comparison	Group 2: Fiberoptic phototherapy Fiberoptic phototherapy (Ohmeda BiliBlanket) consisted of a halogen lamp illuminating a flat mat using a fiberoptic attachment containing 2400 optic givers woven into the mat. Baby was naked. The illuminating part of the mat is 11 X13 cm. The light range is in the 400 – 550 nm range. Irradiance level was 35microW/cm2/nm. If TSB levels increased above predetermined cut-offs double phototherapy was started using conventional phototherapy as above.
Length of follow up	Not reported
Location	Netherlands
Outcomes measures and effect size	Need exchange transfusions: Group 1: 3/68; Group 2: 4/56 Median duration of phototherapy Group 1 = 114 hours; Group 2 = 118 hours

Bibliographic reference **Q1: Old**	**Author: Van Kaam A** **Fibre optic versus conventional phototherapy for hyperbilirubinaemia in preterm infants** **Year: 1998** **ID: 154**
	Mean change in TSB: Group 1: -2 ± 25 micromol/litre; Group 2: -2 ± 20 micromol/litre Mortality during phototherapy: Group 1: 2/68; Group 2: 2/56
Source of funding	Not reported
Comments	Blinding: Not reported Randomisation: Not reported but sealed envelopes used ITT conducted.

1

Bibliographic reference **Q1: Old**	**Author: Costello S** **BiliBlanket phototherapy system versus conventional phototherapy: A randomized controlled trial in preterm infants.** **Year: 1995** **ID: 156**
Study type	RCT
Aim	This study compares the use of standard overhead fluorescent phototherapy units with the BiliBlanket a woven fibreoptic pad which delivers high intensity light with no ultraviolet or infrared irradiation in the treatment of jaundice in preterm infants.
Patient characteristics	Inclusion: Gestational age between 27 and 36 weeks, TSB > 125 micromol/litre) (increased with age (hours) and birthweight Exclusion: Not reported
Number of Patients	N = 44 (conventional = 24, Fiberoptic Biliblanket = 20) Demographics: Gender (M/F): Not reported Mean GA (weeks, range): Conventional = 32.1 (27-36); Fiberoptic = 31.9 (27-36) Mean birthweight (g, range): Conventional = 1731 (941-2448); Fiberoptic = 1474 (840-2259) Mean age at entry to study (hour, range): Conventional = 63 (22-142); Fiberoptic = 49 (15-96)

Bibliographic reference **Q1: Old**	**Author: Costello S** **BiliBlanket phototherapy system versus conventional phototherapy: A randomized controlled trial in preterm infants.** **Year: 1995** **ID: 156**
	Mean TSB: Not reported
Intervention	Group 1: Conventional Phototherapy Conventional phototherapy consisted of a standard system of four white and 4 blue fluorescent lamps 50cm above the baby with an intensity of 8 microW/cm2/nm
Comparison	Group 2: Fiberoptic phototherapy Fiberoptic phototherapy (BiliBlanket) with a constant setting of 35microW/cm2/nm. Baby was nursed in an open cot or isolette and turned at regular intervals from prone to supine positions. Eyes pads were used for babies < 1500gms.
Length of follow up	Not reported.
Location	Australia
Outcomes measures and effect size	Treatment failure (need double phototherapy): Group 1: 3/24; Group 2: 1/20 Mean duration of phototherapy (hour, mean & SD) Group 1: 44.0 ± 42.8 hours; Group 2: 42.0 ± 39.1 hours Side effects: Group 1: 0/24; Group 2: 0/20 Max TSB: Group 1: 210 ± 58 micromol/litre; Group 2: 198 ± 53 micromol/litre
Source of funding	Not reported.
Comments	Blinding: Not reported Randomisation: Lottery method

1

Bibliographic reference **Q1: Old**	**Author: Bertini G** **Transepidermal water loss and cerebral hemodynamics in preterm infants: conventional versus LED phototherapy.** **Year: 2008** **ID: 159**
Study type	RCT
Aim	To evaluate whether high-intensity gallium nitride light-emitting diode (LED) phototherapy (LPT) influences transepidermal water loss (TEWL) and cerebral hemodynamics in preterm neonates in comparison with conventional phototherapy (CPT).
Patient characteristics	Inclusion: TSB ≥ 171 micromol/litre, Gestational ages < 34 weeks, Age < 7days, Did not require respiratory support, Clinically stable Exclusion: Malformations, Perinatal asphyxia, Patent ductus arteriosus, intracranial haemorrhage, hypotension, Hypertension, Infection, Anemia (venous Hb< 10g/dl), Polycythemia (venous Hb> 22 g/dl), Infants receiving cardiovascular drugs.
Number of Patients	N = 31 (conventional = 14, LED = 17) Demographics: Gender (M/F): Not reported Mean GA (week, SD): conventional = 31.3±2.1, LED = 30.2±1.8 Mean BW (g, SD): conventional = 1,191±262, LED = 1,193±225 Mean age at entry to study (hour, SD): conventional = 60±10, LED = 68±18 Mean TSB baseline (umol/L, SD): conventional = 204±14, LED = 197±17
Intervention	Group 1: Conventional phototherapy Conventional phototherapy (Photo-Therapie 800) incorporating a metal vapour discharge blue lamp with two filters (an infrared cut-off filter and a Plexiglas ultraviolet cut-off filter). 20cm above the baby.
Comparison	Group 2: LED Phototherapy LED phototherapy (Natus NeoBlue system). Light range 450–470nm spectrum. Irradiance was at the intensive setting at 30–35 microW/cm2/nm. Unit was placed 30cm above the baby. All babies were placed in incubators with a thermo-monitoring system to maintain a normal body temperature (36.5oC) at a relative humidity of 60%. Babies received full enteral feeding with human milk.

Bibliographic reference **Q1: Old**	**Author: Bertini G** **Transepidermal water loss and cerebral hemodynamics in preterm infants: conventional versus LED phototherapy.** **Year: 2008** **ID: 159**
	Babies were naked except for eye patches and were in a supine position. Phototherapy discontinued at < 145 micromol/litre
Length of follow up	Not reported
Location	Italy
Outcomes measures and effect size	*All infants were studied using cerebral Doppler ultrasound immediately before phototherapy (time 0), 30 min (time 1), 1–6 h (time 2), and 12–24 h (time 3) after the start of phototherapy, and 6–12 h after discontinuing phototherapy (time 4).* Mean duration of phototherapy: Group 1: 38.7 ± 5.0 hours; Group 2: 34.0 ± 12.0 hours Adverse effects (transepidermal water loss [TEWL]) after 12-24 hrs of phototherapy (ml/m^2/hour, SD): Conventional = 20.94±3.21 ml/m^2/h, LED = 14.45±3.68 ml/m^2/h
Source of funding	Not reported
Comments	Blinding: Not reported Randomisation: Not reported but sealed envelopes used

1

Bibliographic reference **Q1: Old**	**Author: Seidman D** **A new blue light-emitting phototherapy device: a prospective randomised controlled study.** **Year: 2000** **ID: 143**
Study type	RCT
Aim	To evaluate the efficacy of a new phototherapy light source with a narrow luminous blue spectrum.
Patient characteristics	Inclusion: Full-term (Gestational age > 37 weeks), Jaundice according to AAP criteria for phototherapy Exclusion: None reported
Number of Patients	N = 69 (conventional = 35, LED = 34)

Bibliographic reference **Q1: Old**	**Author: Seidman D** **A new blue light-emitting phototherapy device: a prospective randomised controlled study.** **Year: 2000** **ID: 143**
	Demographics: Gender (M/F): Not reported Mean GA: Not reported Mean BW: Not reported Age at entry to study: Not reported Mean TSB: 251 ± 77 micromol/litre
Intervention	Group 1: Conventional phototherapy Conventional phototherapy (Micro-lites PTL 68–1) units equipped with 3 halogen quartz bulbs. Irradiance was 5–6 microW/cm2/nm.
Comparison	Group 2: LED phototherapy LED phototherapy consisted of 6 focussed arrays each with 100 3-mm blue LED's. Unit was placed 50cm above the baby, to achieve an irradiance of 5–6microW/cm2/nm. All babies were placed in a crib and were naked except for diapers and eye coverings.
Length of follow up	Not reported
Location	October 1997 through March 1998 at Bikur-Cholim and Misgav-Ladach community hospitals in Jerusalem, Israel.
Outcomes measures and effect size	Total serum bilirubin level was determined in capillary blood samples obtained by heel stick when the newborn appeared clinically jaundiced, and the test was repealed every 4 to 6 hours. Mean duration of phototherapy (hour, mean & SD): Group 1: 32.0 ± 17.0 hours; Group 2: 31.0 ± 17.0 hours, p=0.93 Mean change in TSB (umol/L/h, mean & SD): Group 1: -2.07 ± 3.03 micromol/litre/h; Group 2: -2.87 ± 2.44 micromol/litre/h, p=0.94 Side effects (nausea or dizziness): Group 1: 0/35; Group 2: 0/34

Bibliographic reference **Q1: Old**	**Author: Seidman D** **A new blue light-emitting phototherapy device: a prospective randomised controlled study.** **Year: 2000** **ID: 143**
Source of funding	Not reported
Comments	Blinding: Open label study Randomisation: Computer generated

1

Bibliographic reference **Q1: Old**	**Author: Seidman D** **A Prospective Randomized Controlled Study of Phototherapy Using Blue and Blue-Green Light-Emitting Devices, and Conventional Halogen-Quartz Phototherapy.** **Year: 2003** **ID: 144**
Study type	RCT
Aim	To determine the efficacy of blue versus blue-green phototherapy using new light sources with narrow luminous spectra. The devices made of high intensity gallium nitride light-emitting diodes (LEDs) were also compared to conventional halogen-quartz bulbs phototherapy.
Patient characteristics	Inclusion: AAP criteria for phototherapy, but otherwise healthy term infants. Exclusion: Not reported
Number of Patients	N = 114 (conventional = 57, LED blue = 25, LED blue-green = 22) Demographics: Gender (M/F): Not reported Mean GA (weeks, SD): conventional = 39.4±1.7, LED blue = 39.3±1.4, LED blue-green = 39.9±1.4 Mean BW: Not reported Mean age at entry to study (hour, SD): conventional = 60.4±40.8, LED blue = 48.4±27.2, LED blue-green = 46.2±31.3 Mean TSB (umol/L, SD): conventional = 258±77, LED blue = 245±65, LED blue-green = 243±74 Phototherapy was discontinued when at least two consecutive total serum bilirubin (TSB) measurements showed no increase in TSB levels.
Intervention	Group 1: Conventional phototherapy

Bibliographic reference **Q1: Old**	**Author: Seidman D** **A Prospective Randomized Controlled Study of Phototherapy Using Blue and Blue-Green Light-Emitting Devices, and Conventional Halogen-Quartz Phototherapy.** **Year: 2003** **ID: 144**
	Conventional phototherapy (Air Shields Micro-lites PTL 68–1) units equipped with 3 halogen quartz bulbs. Irradiance was 5–6 microW/cm2/nm.
Comparison	Group 2: LED phototherapy – Blue Blue LED phototherapy consisted of 6 focussed arrays each with 100 3-mm blue LED's. Peak wavelength was 459nm with a half spectral width of 22nm. Unit was placed 50cm above the baby, to achieve an irradiance of 5–6microW/cm2/nm. Group 3: LED Phototherapy - Blue-Green Blue-Green LED phototherapy consisted of 6 focussed arrays each with 100 3-mm blue-green LED's. Peak wavelength was 505nm with a half spectral width of 38nm. Unit was placed 50cm above the baby, to achieve an irradiance of 5–6microW/cm2/nm. All babies were placed in open cribs and were naked except for diapers and eye coverings.
Length of follow up	Not reported
Location	Israel
Outcomes measures and effect size	Mean duration of phototherapy Group 1: 35.4 ± 20.2 hours; Group 2: 31.6 ± 19.6 hours; Group 3: 39.2 ± 25.5 hours Mean decrease in TSB (in umol/L per hour, SD): conventional = -2.42±3.03, LED blue = -2.82±2.44, LED blue-green = -1.55±3.54 No side effects, such as erythema, were noted in any of the newborns. The nurses who cared for the infants did not complain of nausea or dizziness when caring for the babies under the blue LED light. However, both nurses and parents noted that the blue-green lights gave a more disturbing hue to the newborn's skin than the blue or halogen-quartz lamps.
Source of funding	Not reported
Comments	Blinding: Not reported Randomisation: Computer generated random table.

1

Bibliographic reference **Q1: Old**	**Author: Martins B** **Efficacy of new microprocessed phototherapy system with five high intensity light emitting diodes (Super LED).** **Year: 2007** **ID: 158**
Study type	RCT
Aim	To evaluate the efficacy of a microprocessed phototherapy (PT) system with five high intensity light emitting diodes (Super LED) for the treatment of neonatal hyperbilirubinemia of premature infants.
Patient characteristics	Inclusion: Preterm newborn infants, with birth weight of more than 1,000g who need for phototherapy according to birthweight Exclusion: Direct bilirubin > 34 micromol/litre, Haemolytic jaundice, Ecchymosis, Malformations, Congenital infection
Number of Patients	N = 88 (conventional = 44; LED = 44) Demographics: Gender (M/F): conventional = 30/14; LED = 28/16 Mean GA (week, SD): conventional = 33.8 (1.8); LED = 33.4 (2.0) Mean BW (g, SD): conventional = 2032 (483) LED = 1965 (597) Mean age at entry to study (hour, SD): conventional = 70.8 (25) LED = 65.4 (26)
Intervention	Group 1: Conventional Phototherapy Conventional phototherapy consisted of a single quartz-halogen lamp, with a dichroic reflector, positioned 50cm from the baby and illuminating a circle of 18cm diameter. Mean irradiance was 21 ± 6microW/cm2/nm.
Comparison	Group 2: LED phototherapy LED phototherapy consisted of the Super LED system positioned 30cm from the patient and illuminating an elliptical area of 38cm x 27cm diameter. Mean irradiance was 37 ± 9microW/cm2/nm. Phototherapy discontinued when TSB levels decreased 30% from original levels. Treatment was considered to have failed if TSB continued to rise and reached a level 30% below TSB levels required for exchange transfusion.
Length of follow up	Not reported
Location	Brazil

Bibliographic reference **Q1: Old**	**Author: Martins B** **Efficacy of new microprocessed phototherapy system with five high intensity light emitting diodes (Super LED).** **Year: 2007** **ID: 158**
Outcomes measures and effect size	Mean duration of phototherapy Group 1 = 63.8 ± 37 hours; Group 2 = 36.8 ± 21 hours Mean TSB during first 24 hours of phototherapy (mg/dL, SD) Group 1 = 9.6 (2.4); Group 2 = 7.2 (2.5) Treatment failure (rebound jaundice): Group 1 = 8/44; Group = 12/44 None of the patients studied exhibited treatment failure (TSB continues to rise despite phototherapy) or required exchange transfusion. None of the patients exhibited temperature instability or skin rash during the study period.
Source of funding	Not reported
Comments	Blinding: Not reported Randomisation method: Not reported

1

Bibliographic reference **Q1: New**	**Author: Surmeli-Onay (2013)** **Phototherapy Rash in Newborn Infants: Does It Differ Between Conventional and Light Emitting Diode Phototherapy?** **ID:**
Study type	RCT
Aim	To evaluate the incidence and severity of acute skin eruptions caused by conventional phototherapy or LED phototherapy in jaundiced newborn infants.
Patient characteristics	*Inclusion:* • Pathologic hyperbilirubinemia was defined as any serum indirect (unconjugated) bilirubin level needing treatment with phototherapy during the first week of life based on the 2004 AAP hyperbilirubinemia treatment guidelines for infants who were ≥35 weeks of gestation and the management for the infants who were <35 weeks of gestation. • Preterm infants (gestational age <37 wks) who required phototherapy in the first week of life and without skin lesions (inherited or acquired) before phototherapy were included in the study.

Bibliographic reference Q1: New	**Author: Surmeli-Onay (2013)** **Phototherapy Rash in Newborn Infants: Does It Differ Between Conventional and Light Emitting Diode Phototherapy?** **ID:**
	Exclusion: • Infants with congenital malformations, congenital intrauterine infections and inherited metabolic diseases were excluded.
Number of Patients	N=58 (CP = 25; LEDP = 33) *Baseline characteristics:* Gender (male/female): CP = 16/9; LEDP = 17/16 Gestational age (wks, mean, SD): CP = 30.9 (2.1); LEDP = 31.1 (2.2) Age at beginning of phototherapy (day, mean, SD): CP = 3.1 (1.6); LEDP = 2.4 (1.4) Birth weight (g, mean, SD): CP = 1460 (540); LEDP = 1493 (407)
Intervention	Conventional phototherapy (CP) Standard phototherapy units (Ertunc Ozcan IC100 Phototherapy device, Ertunc Ozcan, Ankara, Turkey) consisting of two white lamps and two blue lamps with a wavelength of 420 to 480 nm placed 30 cm above the infant.
Comparison	LED phototherapy (LEDP) LEDs device (neoBLUE® LED phototherapy system, Natus Medical, San Carlos, CA) with a wavelength of 450 to 470 nm placed 30 cm above the infant. • Brief periods of discontinuation of phototherapy for feeding or diaper care of the infants were not excluded when calculating the total duration of phototherapy. • Phototherapy was discontinued when the serum indirect bilirubin level decreased below the phototherapy level on the indicated curve. • No skin lotion or oil was applied to the infants before or during phototherapy.
Length of follow up	Not reported.
Location	Neonatal intensive care unit (NICU) of Hacettepe University IhsanDogramaci Childrens' Hospital in Turkey, between May 2011 and January 2012.
Outcomes measures and effect size	*TSB before phototherapy (mg/dL), mean (SD):* CP = 9.2 (3.3); LEDP = 7.9 (2.4) *TSB after 24hrs phototherapy (mg/dL), mean (SD):* CP = 7.5 (3.0); LEDP = 6.2 (2.5) [mean decrease from baseline: CP = -1.7; LEDP = -1.7] *Duration of phototherapy (hrs, mean, SD):*

Bibliographic reference **Q1: New**	**Author: Surmeli-Onay (2013)** **Phototherapy Rash in Newborn Infants: Does It Differ Between Conventional and Light Emitting Diode Phototherapy?** **ID:**
	CP = 30.4 (9.6); LEDP = 31.8 (15.6) *Skin eruption:* CP = 9/25; LED = 11/33, RR = *Mortality:* CP = 1/25; LEDP = 5/33, RR =
Source of funding	Not reported.
Comments	Open-label, sealed envelopes to assign infants.

1

Bibliographic reference **Q1: New**	**Author: Viau-Colindres (2012)** **Prospective Randomized Controlled Study Comparing Low-Cost LED and Conventional Phototherapy for Treatment of Neonatal Hyperbilirubinemia.** **ID:**
Study type	RCT
Aim	To evaluate whether light emitting diode (LED) phototherapy using a low-cost set of lights is as effective as conventional phototherapy in treating hyperbilirubinemia in neonates.
Patient characteristics	*Inclusion:* • Pre-term neonates with neonatal hyperbilirubinemia and indication for phototherapy according to AAP criteria were recruited to participate. Neonates were eligible to participate if their total bilirubin serum concentration was above the cut-off line for their age group, according to their hours of life. *Exclusion:* • Gestational age <32 weeks or >38 weeks; birth weight <1000 g or >2500 g; cholestatic jaundice, defined as direct bilirubin >20% of total bilirubin levels; with other diagnosis, such as sepsis, or requiring ventilation; lack of informed consent.
Number of Patients	N = 45 (BF = 15; HL = 15; LEDP = 15) *Baseline characteristics:* Gender (male/female): BF = 4/11; HL = 7/8; LEDP = 8/7 Gestational age (wks, mean, SD): BF = 34.8 (1.7); HL = 35.7 (1.4); LEDP = 35.3 (1.2) Baseline TSB (mg/dL) [mean as plotted from a graph]: BF = 11.5; HL = 11.5; LEDP = 12.5
Intervention	Conventional phototherapy: Blue fluorescent (BF) or Halogen (HL)

Bibliographic reference **Q1: New**	**Author: Viau-Colindres (2012)** **Prospective Randomized Controlled Study Comparing Low-Cost LED and Conventional Phototherapy for Treatment of Neonatal Hyperbilirubinemia.** **ID:**
	Standard phototherapy using blue fluorescent light and halogen light. • Halogen light phototherapy was administered with an Air Shields Micro-lite model PPT 68-1, series 2. This system has three EXZ halogens lamps, of high intensity quartz. • The blue fluorescent light phototherapy was administered with a Medix phototherapy lamp, model LU-6T (S|N 568-06), which uses six blue fluorescent tubes.
Comparison	LED phototherapy (LEDP) • Low-cost LED phototherapy lights that can be built in several hours using off-the-shelf parts, a printed circuit board and a wood frame. • The LED-based phototherapy lights were built using eighty 10mm blue LEDs that emit a dominant wavelength of 470 nm. The LEDs had a half-spectral width of 20nm with a 20◦ half-angle directivity. • The LEDs were arranged in eight strips of 10 LEDs each. If a single LED fails, the remaining LEDs still light. The LEDs illuminated an area of about 350 cm^2 at a distance of 25 cm from the lights. The peak irradiance measured at the centre of the illuminated area was 25 $\mu Wcm^{-2}nm^{-1}$. The average irradiance across the regions of the light spot that were>8 $\mu Wcm^{-2}nm^{-1}$ was 14 $\mu Wcm^{-2}nm^{-1}$. All patients were placed in incubators, in supine position and fully exposed to the light except for the diaper area and eye region. The phototherapy devices were placed at a distance specified by the manufacturers.
Length of follow up	Not reported.
Location	Neonatal ward of Roosevelt Hospital in Guatemala City, Guatemala.
Outcomes measures and effect size	*TSB (mg/dL) 24hrs post therapy [mean as plotted from a graph]:* BF = 7.0; HL = 6.75; LEDP = 6.5, p>0.05 *Rate of decrease in TSB (mg/dL/hour) [mean as plotted from a graph]:* BF = 0.045; HL = 0.055; LEDP = 0.057, p>0.05 *Duration of phototherapy (hours) [mean as plotted from a graph]:* BF = 108; HL = 92; LEDP = 110, p>0.05
Source of funding	Not reported.
Comments	A random distribution of patients into groups was completed, use of closed envelopes.

1

Bibliographic reference **Q1: New**	**Author: Demirel (2010)** **Comparison of total oxidant/antioxidant status in unconjugated hyperbilirubinemia of newborn before and after conventional and LED phototherapy: A prospective randomized controlled trial.** **ID:**
Study type	RCT
Aim	To evaluate and compare the oxidant and antioxidant status of hyperbilirubinemic infants before and after the two forms of phototherapy: conventional and LED phototherapy, in order to identify the optimal treatment method.
Patient characteristics	*Inclusion:* • Healthy, term and late-preterm (≥35 weeks) newborn infants who exhibited clinically significant indirect hyperbiliribunemia requiring phototherapy in the first week of life (defined as AAP criteria: 25-48 hour serum total bilirubin levels: 15 mg/dL). • 49-72 h: 17 mg/dl; >72 h: >17 mg/dl • Were breast fed and had no pathologic etiological factors for hyperbilirubinemia. • Infants with normal blood counts and peripheral blood smears, normal reticulocyte count, no evidence of blood group iso-immunization, negative result of a direct Coombs test, and normal glucose-6-phosphate dehydrogenize activity were eligible for the study. *Exclusion:* • Infants with severe congenital malformation, positive direct Coombs test, enclosed hemorrhage, maternal diabetes, maternal eclampsia-preeclampsia, birth asphyxia, sepsis, hemolytic type of hyperbilirubinemia due to blood group or Rh incompatibility and those in whom the total serum bilirubin (TSB) level rose by more than 5 mg/dl per day or was higher than 20 mg/dL within the first 24 hours after birth.
Number of Patients	N = 60 (CP = 30; LEDP = 30) *Baseline characteristics:* Gender (female/male): CP = 19/11; LEDP = 15/15 Gestational age (wks, mean, SD): CP = 37.8 (1.07); LEDP = 37.9 (1.04) Birth weight (g, mean, SD): CP = 3044 (375); LEDP = 3044 (364) Age at the start of phototherapy (hrs, mean, SD): CP = 72 (26); LEDP = 70 (30)
Intervention	Conventional phototherapy (CP) The AMS Phototherapy System (intensity 12-16 µW/cm2/nm, spectrum 430-470 nm, consisting of six fluorescent lamps) was used.
Comparison	LED phototherapy (LEDP) For LED phototherapy, the Neoblue® LED phototherapy system (Natus Medical inc., San Carlos, CA, USA, intensity: 30

Bibliographic reference **Q1: New**	**Author: Demirel (2010)** **Comparison of total oxidant/antioxidant status in unconjugated hyperbilirubinemia of newborn before and after conventional and LED phototherapy: A prospective randomized controlled trial.** **ID:**
	µW/cm2/nm, spectrum 450-470 nm) was used. The system was placed over the infants, at a distance of 30 cm. All infants were unclothed except for their eyes and genital region. All infants were exposed to continuous phototherapy, except while feeding and cleaning. The irradiance of the lamps was measured weekly and replaced if necessary. Phototherapy was stopped when two consecutive serum total bilirubin levels, measured 6 hours apart were below 2 mg/dL from the lowest limit for phototherapy.
Length of follow up	Not reported.
Location	A tertiary neonatal intensive care unit in Turkey, from May 2009 to March 2010.
Outcomes measures and effect size	*TSB baseline (mg/dL, mean, SD):* CP = 18.0 (2.3); LEDP = 18.1 (2.7) *TSB at the termination of phototherapy (mg/dL, mean, SD):* CP = 11.0 (1.4); LEDP = 9.9 (1.7) [mean decrease from baseline: CP = -9.0; LEDP = -8.2] *Duration of phototherapy (hrs, mean, SD):* CP = 36 (12); LEDP = 32 (9)
Source of funding	Not reported.
Comments	Randomly assigned by the neonatal staff.

1

Bibliographic reference **Q1: New**	**Author: Kumar (2010)** **Light-emitting Diodes versus Compact Fluorescent Tubes for Phototherapy in Neonatal Jaundice: A Multi-centre Randomized Controlled Trial** **ID:**
Study type	RCT
Aim	To evaluate whether light-emitting diode (LED) phototherapy is as efficacious as compact fluorescent tube (CFT) phototherapy for the treatment of non-hemolytic jaundice in healthy term and late preterm neonates.
Patient characteristics	*Inclusion:* • Newborn infants born at 35 or more completed weeks of gestation were eligible for enrolment, if they developed hyperbilirubinemia needing phototherapy within first 7 days of life. The decision to start phototherapy was made by bedside physicians on the basis of the age of the baby in hours and STB levels, as per American Academy of Paediatrics guidelines.

Bibliographic reference **Q1: New**	**Author: Kumar (2010)** **Light-emitting Diodes versus Compact Fluorescent Tubes for Phototherapy in Neonatal Jaundice: A Multi-centre Randomized Controlled Trial** **ID:**
	Exclusion: • Infants with perinatal asphyxia (Apgar score <4 at 1 minute or <7 at 5 minute), onset of jaundice within 24 h of age, evidence of hemolysis (positive direct Coombs test), rhesus hemolytic disease, culture-positive or clinical sepsis, need for exchange transfusion at the time of enrolment, and major congenital malformations.
Number of Patients	N = 272 (CP = 130; LEDP = 142) *Baseline characteristics:* Gender (male/female): CP = 73/57; LEDP = 77/65 Gestation (wks, mean, SD): CP = 37.6 (1.4); LEDP = 37.6 (1.4) Birth weight (g, mean, SD): CP = 2771 (489); LEDP = 2807 (458) Age at the beginning of phototherapy (hrs, mean, SD): CP = 81.4 (32.5); LEDP = 81.7 (35.6)
Intervention	Conventional phototherapy (CP) Commercially available CFT units consisting of 6 special blue compact fluorescent bulbs (18W, OSRAM special blue lamp) were used for the study.
Comparison	LED phototherapy (LEDP) LED phototherapy units (Srichakra Scientifics, Hyderabad) had multiple LED bulbs arranged in an area of about 20×15 cm and showed peak emission wavelength between 461 to 467 nm. • In both the groups, each enrolled neonate received phototherapy using a single overhead phototherapy unit. A distance of 25-30 cm was maintained between the baby and the bulb/lamp surface for both type of units. • Site investigators were free to provide additional therapy for hyperbilirubinemia like fluid/feed supplementation and phenobarbitone. • Radiant heaters or blowers were used as and when required. Phototherapy was stopped when two consecutive STB levels, measured 6 hours apart were less than 15 mg/dL.
Length of follow up	Not reported.
Location	Four tertiary care neonatal units across India, from November 2007 to July 2008.

Bibliographic reference **Q1: New**	**Author: Kumar (2010)** **Light-emitting Diodes versus Compact Fluorescent Tubes for Phototherapy in Neonatal Jaundice: A Multi-centre Randomized Controlled Trial** **ID:**
Outcomes measures and effect size	*TSB baseline (mg/dL, mean, SD):* CP = 16.9 (2.5); LEDP = 16.8 (2.4) *TSB at the termination of phototherapy (mg/dL, mean, SD):* CP = 12.3 (1.9); LEDP = 12.1 (2.1) [mean decrease from baseline: CP = -4.6; LEDP = -4.7] *Duration of phototherapy (hrs, median, IQR):* CP = 25 (22-36); LEDP = 26 (22-36), p=0.44 *Mean (SD) rates of decrease of TSB during phototherapy (mg/dL):* CP = 0.19 (0.14); LEDP = 0.19 (0.13), p=0.78 *Failure of phototherapy (defined as TSB >20 mg/dL):* CP = 3/130; 6/142, RR = *Exchange transfusion:* CP = 0/130; 2/142, RR = *Rebound increase in TSB needing phototherapy:* CP = 7/130; 8/142, RR =
Source of funding	The prototype LED phototherapy units at all sites were provided by Srichakra Scientifics, Hyderabad, free of cost. CFL unit at AIIMS, New Delhi, was provided by Phoenix Medical Systems, Chennai, free of cost.
Comments	• Open-label multi-centre randomized controlled trial, a web-based random number generator was used for block randomization stratified for each centre. • The site investigator allocated the group by opening serially numbered, opaque, sealed, identical envelopes containing the treatment group allocation after obtaining the informed consent.

1

Bibliographic reference **Q1: New**	**Author: Ngerncham (2012)** **Effectiveness of Conventional Phototherapy versus Super Light-Emitting Diodes Phototherapy in Neonatal Hyperbilirubinemia.** **ID:**
Study type	RCT
Aim	To compare the effectiveness of two phototherapy devices in reducing plasma bilirubin and duration of phototherapy in non-severe hyperbilirubinemia.
Patient	*Inclusion:*

Bibliographic reference **Q1: New**	**Author: Ngerncham (2012)** **Effectiveness of Conventional Phototherapy versus Super Light-Emitting Diodes Phototherapy in Neonatal Hyperbilirubinemia.** **ID:**
characteristics	• Healthy infants aged between 1- and 5-days old with non-severe hyperbilirubinemia, but to a level requiring phototherapy, were recruited. *Exclusion:* • Infants with severe hyperbilirubinemia, which was defined as phototherapy indicated within the first 24 hours of life or plasma bilirubin within 2 mg/dL less than the level of exchange transfusion, were excluded. The AAP guidelines for phototherapy and exchange transfusion criteria were used.
Number of Patients	N = 40 (CP = 20; LEDP = 20) *Baseline characteristics:* Gender (male/female): CP = 14/6; LEDP = 12/8 Gestational age (wks, mean, SD): CP = 38.1 (1.5); LEDP = 37.9 (1.6) Age at the beginning of phototherapy (hrs, median IQR): CP = 71.0 (58.3-84.3); LEDP = 67.0 (51.0-71.0) TSB at the beginning of phototherapy (mg/dL, median IQR): CP = 14.5 (14.0-15.6); LEDP = 14.2 (12.5-15.0)
Intervention	Conventional phototherapy (CP) The phototherapy device used in the CP was “blue-light”, with 6 special blue fluorescent tubes (“Deep blue”, Thai Toshiba Electric Company, 18 watts) in a 33 x 61.5 x 12 cm unit, lined with white cloths.
Comparison	LED phototherapy (LEDP) The phototherapy device used in the “LEDs” group was the Bilitron 3006 (Fanem, Sao Paulo, Brazil) with 5 super LEDs in a 11 x 23 x 5 cm unit. • The distance between both devices and the infants was fixed at 30 cm. The spectral irradiance of the CP and the Bilitron 3006 were 79 and 40 µW/cm2/nm, respectively. • The room temperature in the nursery was between 28°C and 29°C. • In both groups, double phototherapy with two units was indicated for those whose bilirubin still increased after single phototherapy but did not reach exchange transfusion criteria. • Phototherapy was stopped when two consecutive plasma bilirubin specimens, measured 6 to 12 hours apart, were less than 14 mg/dL. • Re-phototherapy was indicated when bilirubin, checked approximately 6 to 8 hours after phototherapy was stopped, rebounded

Bibliographic reference **Q1: New**	**Author: Ngerncham (2012)** **Effectiveness of Conventional Phototherapy versus Super Light-Emitting Diodes Phototherapy in Neonatal Hyperbilirubinemia.** **ID:**
	to the level requiring phototherapy.
Length of follow up	Not reported.
Location	Siriraj Hospital, Mahidol University, Thailand, between February and April 2007.
Outcomes measures and effect size	*Rate of TSB decreasing (mg/dL, median, IQR):* CP = 0.16 (0.09-0.25); LEDP = 0.10 (0.02-0.17), p=0.03 *Duration of phototherapy (hrs, median, IQR):* CP = 23.0 (19.0-30.8); LEDP = 30.0 (22.3-40.3), p=0.11 *Need for re-phototherapy:* CP = 1/20; LEDP = 0/20, RR = *Complications – Hyperthermia:* CP = 0/20; LEDP = 0/20, RR = N/A *Complications – Hypothermia:* CP = 0/20; LEDP = 2/20, RR = *Complications – Rash:* CP = 0/20; LEDP = 0/20, RR = N/A
Source of funding	Not reported.
Comments	Open-label randomized controlled trial. A web-based randomly permuted block was generated for the study.

G.21 Review question 2

Bibliographic reference **Q2: Old**	**Author: Shinwell E** **Effect of Position Changing on Bilirubin Levels During Phototherapy.** **Year: 2002** **ID: 166**
Study type	RCT
Aim	To examine the effect of turning on serum total bilirubin concentration and on the duration of phototherapy.
Patient characteristics	Inclusion: Full term infants with birth weight >2500 g, serum total bilirubin concentration >18 mg/dl, and start of phototherapy at >48 hours of age. Exclusion:

Bibliographic reference **Q2: Old**	**Author: Shinwell E** **Effect of Position Changing on Bilirubin Levels During Phototherapy.** **Year: 2002** **ID: 166**
	Congenital malformation
Number of Patients	N = 30 (supine = 16, changing = 14) Demographics: Gender (M/F): 8/22 Mean GA (week, SD): supine = 38±1, changing = 38±1 Mean BW (g, SD): supine = 3439±322, changing = 3570±617 Mean age at entry to study (h, SD): supine = 114±33, changing = 93±32 Mean TSB at baseline (mg/dL, SD): supine = 18.7±1, changing = 18.8±1
Intervention	Group 1: Conventional - Supine position Phototherapy was provided using a Fluoro - Lite Phototherapy System (Air Shields, Hatboro, PA) containing two white (True Lite Durotest, 20 W) and two blue (General Electric F20T12-B, 20 W) fluorescent tubes. This system delivered a measured irradiance of 635 W/cm2 (8W/cm2 /nm) at a wavelength of 450 nm (Irradiance meter; Radiometer, Copenhagen, Denmark) when positioned 23–25 cm above the infant's mattress. All babies received identical phototherapy for periods of 150 minutes followed by 30 minute breaks for feeding and routine nursing care. Babies in changing position group were alternated between supine and prone. Serum total bilirubin concentration was measured every 6 hours. Phototherapy discontinued after two consecutive measurements TSB < 239 micromol/litre
Comparison	Group 2: Conventional - Changing positions The turning group were positioned alternately supine or prone every 150 minutes.
Length of follow up	Not reported
Location	Israel
Outcomes measures and effect size	Mean duration of phototherapy Group 1: 28 ± 9 hours; Group 2: 40 ± 15 hours Mean decrease in TSB at first 24 hours from baseline (mg/dL, SD): Group 1 = -5.3 (2.0); Group 2 = -3.9 (2.0)

Bibliographic reference **Q2: Old**	**Author: Shinwell E** **Effect of Position Changing on Bilirubin Levels During Phototherapy.** **Year: 2002** **ID: 166**
	Mean decrease in TSB at first 24 hours from baseline (in %, SD): Group 1 = -29% (8%); Group 2 = -21% (10%)
Source of funding	Not reported
Comments	Blinding: Not reported Randomisation: Not reported but sealed, opaque envelopes selected at random was used

1

Bibliographic reference **Q2: Old**	**Chen C** **Changing position does not improve the efficacy of conventional phototherapy.** **Year: 2002** **ID: 167**
Study type	RCT
Aim	To compare positions of infant during conventional phototherapy.
Patient characteristics	Inclusion: TSB > 256 micromol/litre, Absence of blood group incompatibility, Normal G6PD status, Haemoglobin > 14g/dl Exclusion: Congenital anomalies, Significant bruising, Large cephalhematoma
Number of Patients	N = (51 (supine = 24, changing = 27) Demographics: Gender (M/F): supine = 12/12, changing = 7/20 Mean GA (week, SD): supine = 38.3 (1.2), changing = 38.1 (1.1) Mean BW (g, SD): supine = 3141 (372), changing = 3133 (401) Mean age at entry to study (days, SD): supine = 6.4 (2.0), changing = 5.6 (2.0) Mean TSB: Not reported
Intervention	Group 1: Supine position with conventional phototherapy Phototherapy initiated at TSB ≥ 256 micromol/litre and discontinued at TSB < 171 micromol/litre, with 6 white fluorescent lamps,

Bibliographic reference **Q2: Old**	**Chen C** **Changing position does not improve the efficacy of conventional phototherapy.** **Year: 2002** **ID: 167**
	placed 35cm above the infants. Babies in changing position group were alternated between supine and prone every 120 minutes
Comparison	Group 2: Changing position with conventional phototherapy
Length of follow up	Not reported
Location	Taiwan
Outcomes measures and effect size	Mean duration of phototherapy Group 1: 53.3 ± 17.9 hours; Group 2: 52.8 ± 20.2 hours Mean decrease in TSB per hour (mg/dL/hour, SD): Group 1: -0.14 (0.06); Group 2: -0.14 (0.05) Mean decrease in TSB at 24 hours (in %, SD): Group 1: -24.0 (9.5); Group 2: -26.0 (9.7)
Source of funding	Not reported
Comments	Blinding: Not reported Randomisation: Not reported but sealed envelopes used.

1

Bibliographic reference **Q2: Old**	**Author: Mohammadzadeh A** **Supine versus turning position on bilirubin level during phototherapy in healthy term jaundiced neonates.** **Year: 2004** **ID: 168**
Study type	RCT
Aim	The aim of this study was to determine the effect of routine turning versus supine position on the total serum bilirubin (TSB) concentration during phototherapy.
Patient characteristics	Inclusion: TSB ≥ 256 micromol/litre (49–72 hours); TSB ≥ 291 micromol/litre (> 72 hours) Exclusion:

Bibliographic reference **Q2: Old**	**Author: Mohammadzadeh A** **Supine versus turning position on bilirubin level during phototherapy in healthy term jaundiced neonates.** **Year: 2004** **ID: 168**
	Haemolytic disease, Congenital anomalies, Cephalhaematoma, Metabolic disease
Number of Patients	N = 50 (conventional supine = 25, conventional changing position) Demographics: Gender (M/F) : Not reported Mean GA: Not reported Mean BW: Not reported Age at entry to study: Not reported Mean TSB at start of phototherapy (mg/dL, SD): supine = 18.8 (2.5), changing position = 18.8 (2.1)
Intervention	Group 1: Conventional - Supine position Each phototherapy unit contain 4 blue fluorescent tubes (TL20W/52) at a wavelength of 420 - 480 nm positioned 20 cm above the infant's mattress. All babies received identical phototherapy for periods of 150 minutes followed by 30 minute breaks for feeding and routine nursing care. Babies in changing position group were alternated between supine and prone. Phototherapy discontinued after two consecutive measurements TSB < 239 micromol/litre
Comparison	Group 2: Conventional - Changing position
Length of follow up	Not reported
Location	Iran
Outcomes measures and effect size	Mean decrease in TSB after 24 hours of phototherapy (mg/dL): Supine = 9.3, changing position = 9.2 *no SD was provided.
Source of funding	Not reported
Comments	Blinding: Not reported Randomisation: Not reported

1

Bibliographic reference **Q2: Old**	**Author: Lau S** **Serum bilirubin kinetics in intermittent phototherapy of physiological jaundice.** **Year: 1984** **ID: 172**
Study type	RCT
Aim	To compares the efficiency of three different regimens of phototherapy in jaundiced, term Chinese infants.
Patient characteristics	Inclusion: Full-term, Birthweight > 2500gms, TSB between 190 – 205 micromol/litre Exclusion: Jaundice with known causes
Number of Patients	N = 34 (group 1 = 13, group 2 = 9, group 3 = 12) Demographics: Gender (M/F): Not reported Mean GA (week, SD): Group 1 = 39.5 (1.4), Group 2 = 40.0 (1.8), Group 3 = 40.2 (1.3) Mean BW (kg, SD): Group 1 = 3.26 (0.33), Group 2 = 3.10 (0.43), Group 3 = 3.29 (0.44) Age at entry to study: Not reported Mean TSB at start of phototherapy (umol/L, SD): Group 1 = 201.8 (27.4), Group 2 = 193.2 (34.2), Group 3 = 198.4 (12.0)
Intervention	Group 1: Continuous Phototherapy
Comparison	Group 2: Intermittent Phototherapy – 4 hours on - 4 hours off Group 3: Intermittent Phototherapy – 1 hour on - 3 hours off Phototherapy was administered by a bank of 8 fluorescent lamps (Duro-vita lite, 20 W) in standard units. Irradiance was measured every morning by an IL 444 Radiometer (Spectrum 420-470 nanometer, International Light Inc, USA) at the centre of the mattress. Phototherapy was discontinued when TSB < 171 micromol/litre
Length of follow up	Not reported
Location	Hong Kong
Outcomes measures and effect size	The total serum bilirubin concentration was measured 6 to 8 hourly. Rate of decline in TSB (umol/L/hour), mean (SD) Group 1 = 1.08 (4.10), Group 2 = 1.49 (0.87), Group 3 = 1.09 (0.56)

Bibliographic reference **Q2: Old**	**Author: Lau S** **Serum bilirubin kinetics in intermittent phototherapy of physiological jaundice.** **Year: 1984** **ID: 172**
	Mean duration of phototherapy (hrs, SD): Group 1: 89.9 ± 54.2 hours; Group 2: 86.7 ± 28.9 hours; Group 3: 100.0 ± 61.0 hours
Source of funding	Not reported
Comments	Blinding: Not reported Randomisation method: Not reported

1

Bibliographic reference **Q2: Old**	**Author: Ebbesen F** **Therapeutic effect of turquoise versus blue light with equal irradiance in preterm infants with jaundice.** **Year: 2007** **ID: 160**
Study type	RCT
Aim	To compare the efficiency of turquoise light with that of TL52 blue in treatment of preterm infants with jaundice at the same level of body irradiance.
Patient characteristics	Inclusion: Preterm infants (28 –36.6 weeks), Age > 24 hours, No previous phototherapy, Non-haemolytic hyperbilirubinaemia. The indications for phototherapy followed the guidelines of the Danish Paediatric Society. Exclusion: Not reported
Number of Patients	N = 141 (blue 69, turquoise = 72) Demographics: Gender (M/F): blue = 37/32, turquoise = 43/29 Mean GA (week, SD): blue = 237 (18), turquoise = 234 (17) Mean BW (g, SD): blue = 2095 (635) turquoise = 2061 (579) Mean age at entry to study (hour, SD): blue = 74 (34), turquoise = 74 (30) Mean TSB at start of phototherapy (umol/L, SD): blue = 221 (61), turquoise = 221 (60)
Intervention	Group 1: Blue conventional phototherapy

Bibliographic reference **Q2: Old**	**Author: Ebbesen F** **Therapeutic effect of turquoise versus blue light with equal irradiance in preterm infants with jaundice.** **Year: 2007** **ID: 160**
Comparison	Group 2: Turquoise conventional phototherapy Treatment duration was fixed (24 hours) Phototherapy consisted of either 8 blue fluorescent lamps (20 W, 60 x 3.7cm) 41 cm above the baby or 8 turquoise fluorescent lamps (18 W, 60 x 2.6cm) 41 cm above the baby. Distance from baby was different to ensure irradiance was identical in both groups. Phototherapy was continuous with breaks for feeding etc. Babies were naked except for eye patches and diapers
Length of follow up	Not reported
Location	Denmark
Outcomes measures and effect size	Mean decrease in TSB after 24 hours of phototherapy: Group 1: -78 ± 31 umol/litre; Group 2: -92 ± 31 u/litre
Source of funding	Not reported
Comments	Blinding: Not reported Randomisation: Not stated but sealed envelopes used

1

Bibliographic reference **Q2: Old**	**Author: Eggert P** **On the efficacy of various irradiation regimens in phototherapy of neonatal hyperbilirubinaemia.** **Year: 1988** **ID: 191**
Study type	RCT
Aim	To assess the efficacy of various irradiation regimens in phototherapy of neonatal hyperbilirubinaemia
Patient characteristics	Inclusion: Uncomplicated hyperbilirubinaemia Exclusion: Age < 40 hours with ABO or Rh incompatibility, Babies who received antibiotics
Number of Patients	N = 101 (group 1 = 34, group 2 = 36, group 3 = 31)

Bibliographic reference **Q2: Old**	**Author: Eggert P** **On the efficacy of various irradiation regimens in phototherapy of neonatal hyperbilirubinaemia.** **Year: 1988** **ID: 191**
	Demographics: Gender (M/F): group 1 = 19/15, group 2 = 24/12, group 3 = 19/12 Mean GA (week): 40 weeks for all 3 groups Mean BW (g): group 1 = 3160, group 2 = 3180, group 3 = 3230 Mean age at entry to study (hour): group 1 = 61.5, group 2 = 75.5, group 3 = 70.0 Mean TSB (mg/100ml, SD): group 1 = 14.0 (1.9), group 2 = 14.7 (1.7) group 3 = 13.9 (1.2)
Intervention	Group 1: Conventional Phototherapy Conventional phototherapy consisted of a Drager 76 unit equipped with 6 blue standard fluorescent lights (light range 410 – 520 nm)
Comparison	Group 2: Conventional Phototherapy + white curtains Group 3: Halide Phototherapy In the second group (white curtains) the four outer walls of the incubator were draped in white cloth. The halide phototherapy consisted of a Drager 8000 halide lamp (light range 400 – 580 nm) All babies were treated in intensive care incubators. All phototherapy units were 34cm above the mattress. Babies were naked except for a bikini diaper and blindfolds and were their position was changed every 4 hours. Phototherapy could be interrupted for nursing care and feedings. Babies received oral feedings of either mother's milk or adapted formula and dextrose solution.
Length of follow up	Not reported
Location	Germany
Outcomes measures and effect size	Mean decrease in TSB at 24 hours from baseline (in %, SD): Group 1: -23.4% (9.4); Group 2: -31.6% (9.7); Group 3: -22.6% (9.0)
Source of funding	Not reported
Comments	Blinding: Not reported Randomisation: Not reported

1

Bibliographic reference **Q2: Old**	**Author: Ayyash H** **Green or blue light phototherapy for neonates with hyperbilirubinaemia.** **Year: 1987** **ID: 162**
Study type	RCT
Aim	To compare blue and green light conventional phototherapy.
Patient characteristics	Study 1: Full-term (≥37 weeks) Inclusion: Neonates with jaundice of unknown aetiology Exclusion: Haemolytic jaundice Study 2: Preterm (<37 weeks) Inclusion: Neonates with jaundice of unknown aetiology Exclusion: Haemolytic jaundice
Number of Patients	Study 1: Full-term N = 200 (blue = 100, green = 100) Demographics: Gender (M/F): Not reported Mean GA (weeks, SD): blue conventional = 38.99 (0.127), green conventional = 38.88 (0.131) Mean BW (g, SD): blue conventional = 3397 (44), green conventional = 3391 (43) Mean age at entry to study (hour, SD): blue conventional = 98.53 (3.09), green conventional = 105.00 (2.62) Mean TSB at start of phototherapy (umol/L): blue conventional = 284 (3.2), green conventional = 288 (2.5) Study 2: Preterm N = 62 (blue = 31, green = 31) Demographics: Gender (M/F): Not reported Mean GA (weeks, SD): blue conventional = 34.58 (0.340), green conventional = 34.70 (0.374)

Bibliographic reference **Q2: Old**	**Author: Ayyash H** **Green or blue light phototherapy for neonates with hyperbilirubinaemia.** **Year: 1987** **ID: 162**
	Mean BW (g, SD): blue conventional = 2304 (80), green conventional = 2418 (91) Mean age at entry to study (hour, SD): blue conventional = 83.73 (5.52), green conventional = 87.45 (4.93) Mean TSB at start of phototherapy (umol/L): blue conventional = 227 (9.3), green conventional = 251 (12.7)
Intervention	Group 1: Blue Conventional Phototherapy
Comparison	Group 2: Green Conventional Phototherapy Phototherapy consisted of 5, either green or blue, fluorescent tubes mounted on a conventional phototherapy unit.
Length of follow up	Not reported
Location	Greece
Outcomes measures and effect size	Study 1 – Full-term Mean duration of phototherapy Group 1: 49.88 ± 3.02 hours; Group 2: 42.68 ± 2.74 hours Mean decrease in TSB (umol/L/hour): Group 1: -2.86 (0.17); Group 2: -3.27 (0.22) Study 2 – Preterm Mean duration of phototherapy Group 1: 53.29 ± 5.9 hours; Group 2: 53.26 ± 5.52 hours Mean decrease in TSB (umol/L/hour): Group 1: -2.50 (0.39); Group 2: -2.91 (0.38)
Source of funding	Not reported
Comments	Blinding: Not reported Randomisation: Not reported

1

Bibliographic reference **Q2: Old**	**Author: Amato M** **Clinical usefulness of high intensity green light phototherapy in the treatment of neonatal jaundice** **Year: 1991** **ID: 163**
Study type	RCT
Aim	To compare light bulbs of conventional phototherapy.
Patient characteristics	Inclusion: Idiopathic hyperbilirubinaemia; TSB ≥ 250 micromol/litre Exclusion: Perinatal asphyxia, Apgar < 4 at 1 minute and < 6 at 5 minutes, Signs of haemolytic disease, secondary hyperbilirubinaemia
Number of Patients	N = 30 (conventional blue = 15, conventional green = 15) Demographics: Gender (M/F): conventional blue = 7/8, conventional green = 6/9 Mean GA (weeks, SD): conventional blue = 39 (1.1), conventional green = 39 (1.0) Mean BW (g, SD): conventional blue = 3510 (580), conventional green = 3280 (504) Mean age at entry to study (hour, SD): conventional blue = 72 (23), conventional green = 69 (24)
Intervention	Group 1: Blue Conventional Phototherapy
Comparison	Group 2: Green Conventional Phototherapy Phototherapy consisted of either blue or green fluorescent tubes 30cm above the mattress. The baby was placed naked, except for eye patches and gonadal protection, on a Plexiglas surface. Light spectral range of green tubes was 350–650 nm and 300–600 for the blue tubes. Babies were supplemented with 5% glucose (15 mg/kg per day) Phototherapy discontinued at TSB < 200 micromol/litre Rebound jaundice was a rise of 17 micromol/litre after phototherapy discontinuation
Length of follow up	Not reported
Location	Switzerland
Outcomes measures and effect size	Rebound jaundice: Group 1: 12/15; Group 2: 3/15

Bibliographic reference **Q2: Old**	**Author: Amato M** **Clinical usefulness of high intensity green light phototherapy in the treatment of neonatal jaundice** **Year: 1991** **ID: 163**
	Mean duration of phototherapy Group 1: 34 ± 10 hours; Group 2: 70 ± 23 hours Mean decrease in TSB after 24 hours of phototherapy: Group 1: -90.0 ± 26.4 umol/litre; Group 2: -46.6 ± 28.7 umol/litre
Source of funding	Not reported
Comments	Blinding: Not reported Randomisation: Random numbers table

1

Bibliographic reference **Q2: Old**	**Author: Djokomuljanto S** **Efficacy of phototherapy for neonatal jaundice is increased by the use of low-cost white reflecting curtains.** **Year: 2006** **ID: 190**
Study type	RCT
Aim	To determine whether the addition of low-cost reflecting curtains to a standard phototherapy unit could increase effectiveness of phototherapy for neonatal jaundice.
Patient characteristics	Inclusion: Term babies with uncomplicated jaundice requiring phototherapy Exclusion: TsB approaching criteria for exchange transfusion
Number of Patients	N = 100 (curtains = 51, no curtain = 49) Demographics: Gender (M/F): group 1 = 30/21, group 2 = 26/23 Mean GA: Not reported Mean BW (kg, SD): group 1 = 3.01 (0.49), group 2 = 3.07 (0.44) Mean age at entry to study (day, SD): group 1 = 4.30 (2.08), group 2 = 4.45 (2.07) Mean TSB at baseline (umol/L, SD): group 1 = 262.94 (61.51), group 2 = 264.76 (56.63)

Bibliographic reference **Q2: Old**	**Author: Djokomuljanto S** **Efficacy of phototherapy for neonatal jaundice is increased by the use of low-cost white reflecting curtains.** **Year: 2006** **ID: 190**
Intervention	Group 1: Conventional phototherapy
Comparison	Group 2: Conventional phototherapy + white curtains Conventional phototherapy consisted of Phoenix Medical Systems unit of 6 compact blue fluorescent lamps 45 cm above the baby. Curtains were hung on both sides if the phototherapy unit.
Length of follow up	No reported
Location	Malaysia
Outcomes measures and effect size	Mean decrease in TSB after 4 h of phototherapy (umol/L, SD): Group1 = 27.62 (25.24); group 2 = 4.04 (24.27) (p = 0.001). Median duration of phototherapy = 22 h shorter in group 1, hazard ratio = 0.20 (95%CI: 0.12 to 0.32). None of the babies required phototherapy for rebound hyperbilirubinaemia. None of the babies developed hypothermia or hyperthermia.
Source of funding	No reported
Comments	Blinding: not reported. Randomisation: method not reported.

1

Bibliographic reference **Q2: Old**	**Author: Sivanandan S** **Effect of Sling Application on Efficacy of Phototherapy in Healthy Term Neonates with Non-hemolytic Jaundice: A Randomized Conrolled Trial** **Year: 2009** **ID: 192**
Study type	RCT
Aim	To evaluate the efficacy of white reflecting material (slings) hung from the sides of compact fluorescent lamp (CFL) phototherapy equipment in reducing the duration of phototherapy in healthy term neonates with non-hemolytic jaundice.
Patient	Inclusion:

Bibliographic reference **Q2: Old**	**Author: Sivanandan S** **Effect of Sling Application on Efficacy of Phototherapy in Healthy Term Neonates with Non-hemolytic Jaundice: A Randomized Conrolled Trial** **Year: 2009** **ID: 192**
characteristics	Term babies with nonhaemolytic jaundice on a postnatal ward of a tertiary level neonatal unit, Age ≥ 24 hours and < 20 days, 5 minute Apgar > 6, TSB < 359 micromol/litre Exclusion: Hyperbilirubinaemia requiring exchange transfusion, Rh haemolysis, G6PD deficiency, Evidence of haemolysis, Positive Coombs' test, Major congenital malformation, Culture-positive sepsis, Need of intensive care
Number of Patients	N = 84 (conventional = 42, conventional + slings = 42) Demographics: Gender (M/F): conventional = 22/42, conventional + slings = 25/42 Mean GA (week, SD): conventional = 37±1.0, conventional + slings = 38 ±1.3 Mean BW (g, SD): conventional = 2923±330, conventional + slings = 2790±351 Mean age at entry to study (h, SD): conventional = 73±44, conventional + slings = 65 ±24.9 Mean TSB at start of phototherapy (mg/dL, SD): conventional = 16.1±2.2, conventional + slings = 16.6±2.4
Intervention	Group 1: Conventional phototherapy
Comparison	Group 2: Conventional phototherapy + reflecting slings Conventional phototherapy consisted of Phoenix Medical Systems unit of 4 blue and 2 white compact fluorescent lamps 45 cm above the baby. Light range was425 – 475 nm. The white-reflecting material (the slings) could be hung to the units by Velcro strips. The slings were made up of white plastic sheets with reflecting inner surface. The slings covered three sides of the unit. Treatment failure was defined as TSB > 342 micromol/litre Phototherapy was discontinued if If started after 72 hours of age after two consecutive TSB < 256 micromol/litre If started before 72 hours of age after two consecutive were less than agespecific threshold for phototherapy TSB was measured for rebound after 8 hours

Bibliographic reference **Q2: Old**	**Author: Sivanandan S** **Effect of Sling Application on Efficacy of Phototherapy in Healthy Term Neonates with Non-hemolytic Jaundice: A Randomized Conrolled Trial** **Year: 2009** **ID: 192**
Length of follow up	Not reported
Location	India
Outcomes measures and effect size	Mean decrease in TSB (at 8 hours) (mg/dL/hour, SD): Group 1 = 0.03 (0.47), Group 2 = 0.23 (0.49) Percentage of fall in TSB at 24 hours (%, SD) Group 1 = 13.5 (10.9), Group 2 = 19.5 (23.0) Mean duration of phototherapy (hour, SD) Group 1: 24.9 ± 15.4 hours; Group 2: 23.3 ± 12.9 hours Phototherapy failure Group 1: 52; Group 2: 4/42 None of neonates in either group required exchange transfusion. None of the participants developed hyperthermia, feed intolerance, vomiting, decreased urine output, and skin rashes.
Source of funding	Not reported
Comments	Blinding: Not reported Randomisation: Not reported but sealed, serially numbered, opaque envelopes was used.

1

Bibliographic reference **Q2: Old**	**Author: Mehta S** **RANDOMIZED CONTROLLED TRIAL OF FLUID SUPPLEMENTATION IN TERM NEONATES WITH SEVERE HYPERBILIRUBINEMIA.** **Year: 2005** **ID: 174**
Study type	RCT
Aim	To evaluate the effectiveness of fluid supplementation in decreasing the rate of exchange transfusion and the duration of phototherapy in term neonates with severe non-hemolytic hyperbilirubinemia.

Bibliographic reference **Q2: Old**	**Author: Mehta S** **RANDOMIZED CONTROLLED TRIAL OF FLUID SUPPLEMENTATION IN TERM NEONATES WITH SEVERE HYPERBILIRUBINEMIA.** **Year: 2005** **ID: 174**
Patient characteristics	Inclusion: Hyperbilirubinaemia; TsB > 308 micromol/litre Exclusion: TsB > 427 micromol/litre, Kernicterus, Evidence of hemolysis, Signs of dehydration, Major congenital malformations, Babies on IV fluids
Number of Patients	N = 74 (usual feeds = 37; extra fluids = 37) Demographics: Gender (M/F): Usual feeds = 23/14; extra fluids = 29/8 Mean GA (week, SD): Usual feeds = 37.8 (1.0); extra fluids = 37.5 (0.8) Mean BW (g, SD): Usual feeds = 3022 (463); extra fluids = 2851 (473) Mean age at entry to study: Not reported. Mean TSB at start of phototherapy (umol/L, SD): Usual feeds = 349 (32); extra fluids = 350 (31)
Intervention	Group 1: Conventional Phototherapy + Usual feeds
Comparison	Group 2: Conventional Phototherapy + Usual Feeds + Extra fluids All infants received special blue light phototherapy (Philips TL52, 20W; Philips, The Netherlands). The irradiance to the infant was recorded daily using a flux meter (Minolta, Germany). Extra fluids consisted of IV fluid supplementation with N/5 saline in 5% dextrose for a period of 8 hours before phototherapy. After babies were offered 30mL/kg/day of extra oral feeds (expressed breast milk or formula) until phototherapy discontinued. Phototherapy was discontinued when two TsB values obtain 12 hours apart were < 256 micromol/litre. Exchange transfusion was done if at 4 hours into the study TsB increased by > 34 micromol/litre or if at 8 hours TsB remained > 342 micromol/litre.
Length of follow up	Not reported.
Location	India
Outcomes measures and effect size	Exchange Transfusions Group 1 = 20/37; Group 2 = 6/37

Bibliographic reference **Q2: Old**	**Author: Mehta S** **RANDOMIZED CONTROLLED TRIAL OF FLUID SUPPLEMENTATION IN TERM NEONATES WITH SEVERE HYPERBILIRUBINEMIA.** **Year: 2005** **ID: 174**
	Mean decrease in TSB at the first 8 hours of phototherapy (in % of fall from baseline, SD): Group 1 = -4.0% (9.0) (n = 17); Group 2 = -17.0% (10.0) (n = 32) Mean decrease in TSB at the first 24 hours of phototherapy (in % of fall from baseline, SD): Group 1 = -19.0% (12.0) (n = 17); Group 2 = -27.0% (11.0) (n = 31) Mean duration of treatment: Group 1 = 73 ± 31 hours; Group 2 = 52 ± 18 hours *Exchange transfusion was done if at 4 hours into the study period, TSB increased by > 2 mg/dL (34 mmol/L) over the value at the start of the study, or if at 8 hours into the study period, TSB remained ≥ 20 mg/dL (342 mmol/L).*
Source of funding	Not reported.
Comments	Blinding: Not reported Randomisation: Stratified block randomisation (based on TsB levels) using sealed opaque envelopes

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Bibliographic reference **Q2: Old**	**Author: Boo N** **Randomized controlled trial of oral versus intravenous fluid supplementation on serum bilirubin level during phototherapy of term infants with severe hyperbilirubinaemia.** **Year: 2002** **ID: 175**
Study type	RCT
Aim	To compare the rates of decrease in serum bilirubin levels in severely jaundiced healthy term infants given oral or intravenous fluid supplementation during phototherapy.
Patient characteristics	Inclusion: TSB > 300 micromol/litre with conjugated bilirubin <15% of TSB Exclusion: Sick babies, Major congenital malformations, Conjugated hyperbilirubinaemia, prolonged jaundice
Number of Patients	N = 54 (enteral = 27; enteral + intravenous = 27)

Bibliographic reference **Q2: Old**	**Author: Boo N** **Randomized controlled trial of oral versus intravenous fluid supplementation on serum bilirubin level during phototherapy of term infants with severe hyperbilirubinaemia.** **Year: 2002** **ID: 175**
	Demographics: Gender (M/F): enteral = 18/9; enteral + intravenous = 19/8 Mean GA (week, SD): enteral = 39.3 (1.0); enteral + intravenous = 39.4 (0.9) Mean BW (g, SD): enteral = 3003 (321); enteral + intravenous = 3147 (512) Mean age at entry to study (days, SD): enteral = 6.4 (1.8); enteral + intravenous = 5.2 (2.0) Mean TSB at start of phototherapy (umol/L, SD): enteral = 369 (72); enteral + intravenous = 386 (60)
Intervention	Group 1: Conventional Phototherapy + Enteral feeds alone Enteral feeds group: Formula-fed babies were given 8 divided feeds at 3 hour intervals. Breastfed babies were breastfed on demand. In addition they were given half of the calculated volume of formula feeds given to the formula-fed babies.
Comparison	Group 2: Conventional Phototherapy + 50 % Enteral feeds + 50% Intravenous feeds Enteral + Intravenous group: Formula-fed babies were given half of their 24hour fluid requirement at eight divided feeds at 3hour intervals. The remaining half of their daily fluid requirement was given as continuous intravenous1/5 normal saline and 5% dextrose infusion via a peripheral vein over 24 hours. Breastfed babies were breastfed on demand. Half of their daily fluid requirement was given as continuous intravenous1/5 normal saline and 5% dextrose infusion via a peripheral vein over 24 hours. Two phototherapy units (Madela, Baar, Switzerland - flourescent) were used for each infant; the phototherapy light panels were placed at a distance of 25 cm above the infants in order to achieve an irradiance of 25–35 μW/cm2 per nm. All babies received a daily maintenance fluid level of 90 mL/kg on day 2, 1290 mL/kg on day 3 and 150 mL/kg from day 4 onwards. They were also given an additional 10% of their respective total daily fluid requirement to compensate for the fluid loss.
Length of follow up	Not reported.
Location	Malaysia
Outcomes measures and effect size	Exchange Transfusions Group 1 = 5/27; Group 2 = 8/27 Rate of decrease in indirect serum bilirubin (iSB) per hour (during the first 4 hours) (umol/L, SD):

Bibliographic reference **Q2: Old**	**Author: Boo N** **Randomized controlled trial of oral versus intravenous fluid supplementation on serum bilirubin level during phototherapy of term infants with severe hyperbilirubinaemia.** **Year: 2002** **ID: 175**
	Group 1 -10.4 (4.9); Group 2 = -11.2 (7.4) No infants developed vomiting or abdominal distension during the study period.
Source of funding	Not reported.
Comments	Blinding: Not reported Randomisation: Stratified randomisation (type of feed, hydration status, and TSB levels) using sealed envelopes.

1

Bibliographic reference **Q2: Old**	**Author: Martinez J** **Hyperbilirubinemia in the breast-fed newborn: a controlled trial of four interventions.** **Year: 1993** **ID: 133**
Study type	RCT
Aim	To compare the effect of breast feeding.
Patient characteristics	Inclusion: TSB > 291micromol/litre but otherwise healthy infants delivered between 38 to 41 gestational weeks. Exclusion: Congenital anomalies; Neonatal complications; Birthweight below 10th percentile or above 90th percentile; Venous hematocrit > 65%; Significant bruising; Large cephalhematoma; Haemolytic disease
Number of Patients	N = 74 (breastfeeding = 38, substitute formula = 36) Demographics: Gender (M/F): group 1 = 19/19, group 2 = 23/13 Mean GA (week, SD): group 1 = 39.2 (1.0), group 2 = 39.4 (0.9) Mean BW (g, SD): group 1 = 3424 (374), group 2 = 3359 (371) Age at entry to study: Not reported Mean TSB at start of phototherapy (umol/L, SD): group 1 = 306 (13), group 2 = 308 (13)
Intervention	Group 1: Continue breastfeeding with conventional phototherapy

Bibliographic reference **Q2: Old**	**Author: Martinez J** **Hyperbilirubinemia in the breast-fed newborn: a controlled trial of four interventions.** **Year: 1993** **ID: 133**
Comparison	Group 2: Substitute formula feeds, with conventional phototherapy Conventional Phototherapy consisted of Quartz halide spot unit Irradiance = 10 microwatt/cm^2 Light band = 400 – 480 nm Babies were naked with eyes patched in a bassinet Phototherapy discontinued at TSB < 231 micromol/litre
Length of follow up	Not reported
Location	Argentina
Outcomes measures and effect size	Mean decrease in TSB (at 48 hours) (umol/L, SD): Group 1: -77 ± 41 micromol/litre; Group 2: -65 ± 34 micromol/litre No infant required exchange transfusion.
Source of funding	Not reported
Comments	Blinding: Not reported Randomisation: Computer-generated

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Bibliographic reference **Q2: New**	**Author: Donneborg (2010)** **Effect of infants' position on serum bilirubin level during conventional phototherapy.** **ID:**
Study type	RCT
Aim	To compare the decrease in total serum bilirubin (TSB) concentration during conventional phototherapy in infants treated in supine position exclusively versus infants alternated between exposure in supine and prone position every third hour.
Patient characteristics	*Inclusion:* Neonates with non-haemolytic hyperbilirubinaemia, otherwise healthy at time of inclusion, a gestational age ≥33 weeks, fulfilling the indications for phototherapy, postnatal age >24 h, not having received phototherapy for the last 48 h and being able to be treated in the cradle.

Bibliographic reference Q2: New	**Author: Donneborg (2010)** **Effect of infants' position on serum bilirubin level during conventional phototherapy.** **ID:**
	Exclusion: Not reported.
Number of Patients	N = 112 (alternating = 59; supine = 53) *Baseline characteristics:* Gender (female/male): AP = 25/34; SP = 22/31 Gestational age (days, median 95%CI): AP = 253 (250-259); SP = 259 (256-265) Birth weight (g, medial, 95%CI): AP = 2750 (2480-2941); SP = 2810 (2545-3103)
Intervention	Alternating position (AP) At start of phototherapy, all infants were in supine position, then it was changed every third hour from supine to prone and vice versa. All infants received phototherapy for 24 h.
Comparison	Supine position only (SP) All infants received phototherapy for 24 h. The phototherapy apparatus used for both groups was a neoBLUE LED phototherapy device (Natus Medical Inc., San Carlos, CA, USA) emitting blue light with an emission peak at 470 nm and a bandwidth of 455–485 nm. All infants were treated with light from above, and the distance from the phototherapy apparatus to the mattress was 20 cm.
Length of follow up	Not reported..
Location	Neonatal intensive care unit at Aalborg Hospital, Aarhus University Hospital, Denmark, between 1 March 2008 and 30 June 2009.
Outcomes measures and effect size	TSB (µmol/L) (mean, 95%CI): Start of phototherapy: AP = 294 (280-309); SP = 295 (280-311), p=0.91 After 24 hours of phototherapy: AP = 153 (140-165); SP = 150 (137-163), p=0.75 Decrease in TSB (%) (mean, 95%CI): After 24 hours of phototherapy: AP = 49 (47-51); SP = 50 (47-53), p=0.66
Source of funding	Not reported.
Comments	Randomized equally by sealed opaque envelopes.

1

Bibliographic reference **Q2: New**	**Author: Bhethanabhotla (2013)** **Effect of position of infant during phototherapy in management of hyperbilirubinemia in late preterm and term neonates: a randomized controlled trial.** **ID:**
Study type	RCT
Aim	To evaluate the effect of supine position when compared with periodic change of position during phototherapy in late preterm and term neonates (35 to 42 weeks) with hyperbilirubinemia on the duration of phototherapy.
Patient characteristics	*Inclusion:* • All neonates with neonatal hyperbilirubinemia requiring phototherapy as per AAP nomogram were screened, and those of age 424 h and o14 days were enrolled into the study. *Exclusion:* • Neonates with Rh hemolytic disease, positive direct Coomb's test and major congenital anomalies, Rh-incompatible and ABO-incompatible were excluded.
Number of Patients	N = 100 (supine = 54; turning = 46) *Baseline characteristics:* Male/female: supine = 32/22; turning = 28/18 Gestational age (week, mean & SD): supine = 37.1 (1.2); turning = 37.4 (1.3) Birth weight (g, mean & SD): supine = 2752 (478); turning = 2748 (416) Age at initiation of phototherapy (hours, mean & SD): 86.5 (40.1); turning = 87.0 (45.4)
Intervention	Conventional phototherapy (supine) After enrolment, all neonates were initially nursed in supine position. In the supine group (SG), the neonates were continued in the same position. Phototherapy was stopped when two values of TSB were below the cut-off for age and gestational age as per AAP nomogram for management of hyperbilirubinemia in infants >35 weeks of gestation.
Comparison	Conventional phototherapy (turning) In the turning group (TG), change of position from supine to prone and prone to supine was done every 2 h. • Single surface phototherapy was given using a phototherapy unit which has six light sources (Osram Dulux L 18 W/71, four blue

Bibliographic reference **Q2: New**	**Author: Bhethanabhotla (2013)** **Effect of position of infant during phototherapy in management of hyperbilirubinemia in late preterm and term neonates: a randomized controlled trial.** **ID:**
	compact fluorescent lights and two white compact fluorescent lights). The spectrum of light used was 425 to 475 nm, with the maximum adsorption peak at 450–460 nm. Two separate dedicated phototherapy units were used for the purpose of the study. • Irradiance of the units was checked on 20 random neonates as a pilot study using neo BLUE LED phototherapy radiometer (Natus Medical, San Carlos, CA, USA) and was 20 to 25 $uWcm^{-2}nm^{-1}$. Bulbs were changed when irradiance was <20 $uWcm^{-2}nm^{-1}$. Distance from phototherapy unit was fixed at 25 cm. Exclusive breast feeding was done on demand or every 2 h during the phototherapy in both the groups, and the time duration for feeding was recorded.
Length of follow up	Not reported.
Location	Neonatal intensive care unit at All Institute of Medical Sciences, New Delhi, India from June 2010 to July 2011.
Outcomes measures and effect size	Duration of phototherapy (h; including feeding/nursing time) (mean, SD): Supine = 25.5±8; turning = 24.8±5, mean difference = 0.7 (95%CI: 2.03, 3.44) Duration of phototherapy (h; excluding feeding/nursing time) (mean, SD): Supine = 20.0±7.8; turning = 19.6±4.1, mean difference = 0.4 (95%CI: 2.07, 3.02) TSB at 24 h of phototherapy (mg dl^{-1}) (mean, SD): Supine = 12.53±2.1; turning = 12.57±2.3, mean difference = 0.04 (95%CI: 0.8, 0.9) Rate of fall of bilirubin (mg dl h^{-1}) (mean, SD): Supine = 0.20±0.1; turning = 0.22±0.1, mean difference = 0.02 (95%CI: 0.06, 0.02) There were no side effects of phototherapy in any of the neonates enrolled in the study.
Source of funding	The equipment was provided by Phoenix Medical system and Natus Medical.
Comments	Computer-generated random sequence was used in two gestation strata (35 to 36 + 6 weeks and ≥37 weeks) to either supine or turning every 2-h group. Allocation codes were kept in serially numbered, sealed, and opaque envelopes to ensure concealment and were opened by the duty resident.

1

Bibliographic reference **Q2: New**	**Author: Romagnoli (1988)** **Phototherapy for hyperbilirubinemia in preterm infants: Green versus blue or white light.** **ID:**

Bibliographic reference **Q2: New**	**Author: Romagnoli (1988)** **Phototherapy for hyperbilirubinemia in preterm infants: Green versus blue or white light.** **ID:**
Study type	RCT
Aim	The aim of this study was to compare the clinical effectiveness of green lights to two other readily available and frequently used light sources for the treatment of icteric preterm infants.
Patient characteristics	*Inclusion:* • 60 preterm newborn infants whose gestational age was 34 to 36 weeks, who have neonatal jaundice. • Phototherapy was started when total serum bilirubin levels reached 10 to 12 mg/dl. *Exclusion:* • Infants with haemolytic anemia, neonatal asphyxia, respiratory distress syndrome, sepsis, or malformations, and infants of diabetic mothers. • Infants whose mothers had received any treatment, such as phenobarbital or corticosteroids, that might influence neonatal hyperbilirubinemia were also excluded.
Number of Patients	N = 60 (green light = 20; day light = 20; blue light = 20) *Baseline characteristics:* *Male/female:* Green light = 10/10; day light = 8/12; blue light = 12/8 *Gestational age (week, mean & SD):* Green light = 35.1 (0.7); day light = 35.1 (1.0); blue light = 35.0 (1.4) *Birth weight (g, mean & SD):* Green light = 2120 (399); day light = 2144 (275); blue light = 2126 (296) *Age at start of phototherapy (hour, mean & SD):* Green light = 58 (17); day light = 58 (18); blue light = 57 (18) *Serum bilirubin at start of phototherapy (mg/dL, mean & SD):* Green light = 11.1 (1.14); day light = 11.6 (1.49); blue light = 11.2 (2.02)
Intervention	Conventional phototherapy (green light) *Green light (eight lamps, Sylvania F20T12/G [GTE Sylvania, Inc., Salem, Mass.])* *The total power irradiance reaching the skin of the baby through the double Plexiglas shield of the phototherapy unit and the incubator was 1750 uW/cm^2 for green light.*

Bibliographic reference Q2: New	**Author: Romagnoli (1988)** **Phototherapy for hyperbilirubinemia in preterm infants: Green versus blue or white light.** **ID:**
	Feeding was started at 1 hour of life according to pre-established schedules, and was similar for all the babies. The irradiance was measured by a power meter modified to read radiant flux in the spectral range of 300 to 700 nm with ~4% accuracy.
Comparison	Conventional phototherapy (day light) *Day light (eight lamps, Duro-Test 20TH12 TXC [Duro-Test Corp., North Bergen, N.J.]).* *The total power irradiance reaching the skin of the baby through the double Plexiglas shield of the phototherapy unit and the incubator was 1750 uW/cm^2 for daylight.* Conventional phototherapy (blue light) *Blue light (eight lamps, Philips TC20W/03 T [Philips Electronic Instruments, Inc., Mahwah, N.J.]).* *The total power irradiance reaching the skin of the baby through the double Plexiglas shield of the phototherapy unit and the incubator was 2010 uW/cm^2 for blue light.* All infants in all groups were periodically turned from prone to supine position and vice versa to produce a uniform exposure to the light.
Length of follow up	Conjugated bilirubin measurements were performed on the first, third, and seventh days of life, but only results up to 72 hours were reported in the study.
Location	Rome, Italy.
Outcomes measures and effect size	*Percentage change in serum bilirubin concentration after first 72 hours (mean, SD):* Green light (GL) = -17.2% (2.88); day light (DL) = -23.3% (3.12); blue light (BL) = -34.5 (2.86) GL vs. DL, p<0.05; GL vs BL, p<0.001; DL vs BL, p<0.001
Source of funding	Not reported.
Comments	Only mentioned infants were randomly assigned to the groups.

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Bibliographic reference Q2: New	**Author: Ayyash (1987)** **Green light phototherapy in newborn infants with ABO hemolytic disease.** **ID:**
Study type	RCT
Aim	To evaluate the efficacy of green light versus blue light phototherapy in full-term infants with ABO incompatibility.
Patient	*Inclusion:*

Bibliographic reference **Q2: New**	**Author: Ayyash (1987)** **Green light phototherapy in newborn infants with ABO hemolytic disease.** **ID:**
characteristics	• 83 otherwise normal full-term infants with jaundice caused by ABO incompatibility and with positive Coombs tests. *Exclusion:* • Not reported.
Number of Patients	N = 83 (green light = 42; blue light = 41) *Baseline characteristics:* *Male/female:* Green light = 23/19; blue light = 20/21 *Gestational age (week, mean & SD):* Green light = 38.5 (6.0); blue light = 38.6 (6.2) *Birth weight (g, mean & SD):* Green light = 3475 (547); blue light = 3347 (528) *Age at start of phototherapy (hour, mean & SD):* Green light = 61.0 (5.5); blue light = 58.4 (4.9) *Serum bilirubin at start of phototherapy (mg/dL, mean & SD):* Green light = 16.3 (2.8); blue light = 16.8 (2.9)
Intervention	Conventional phototherapy (green light) Green lights, standard Sylvania F20T12G (green) fluorescent tubes (GTE Sylvania, Inc., Salem, Mass.), were used; they were mounted into conventional phototherapy units with five lamps.
Comparison	Conventional phototherapy (blue light) Blue lights, standard F20T12B (blue) fluorescent tubes (GTE Sylvania, Inc., Salem, Mass.), were used; they were mounted into conventional phototherapy units with five lamps. For both lights, the emission spectra were supplied by the GTE Sylvania AEEE and were confirmed by measurements with a Bausch & Lomb (Rochester, N.Y.) 250 monochromator in conjunction with an EMI 9558 B photomultiplier. Radiance was measured at a distance of 50 cm from the lamps with a research IL700 radiometer that was responsive to wavelengths of 240 to 1100 nm.
Length of follow up	Not reported.

Bibliographic reference **Q2: New**	**Author: Ayyash (1987)** **Green light phototherapy in newborn infants with ABO hemolytic disease.** **ID:**
Location	Athens, Greece.
Outcomes measures and effect size	Routine levels of serum bilirubin were obtained at least every 6 hours before, during, and 48 hours after the termination of phototherapy treatment with a bilirubinometer. Duration of phototherapy (hr, mean & SD): Green light = 84.6 (14.1); blue light = 81.5 (14.2), p>0.05 Serum bilirubin at end of phototherapy (mg/dL, mean & SD): Green light = 12.2 (1.9); blue light = 12.5 (2.0), p>0.05 Rate of rise of serum bilirubin (post-phototherapy rebound) (mg/hr, mean & SD): Green light = 0.07 (0.01); blue light = 0.09 (0.02), p>0.05 Rate of serum bilirubin photo-degradation (mg/hr, mean & SD): Green light = 0.19 (0.03); blue light = 0.17 (0.03), p>0.05
Source of funding	Partially supported by a grant from the National Fellowship Foundation, Athens, Greece.
Comments	The neonates with jaundice were assigned to treatment groups according to a random number sequence.

1

Bibliographic reference **Q2: New**	**Author: Babaei (2013)** **Effect of White Plastic Cover around the Phototherapy Unit on Hyperbilirubinemia in Full Term Neonates.** **ID:**
Study type	RCT
Aim	To determine the effect of adding white plastic cover around the phototherapy unit on hyperbilirubinemia in full term neonates with jaundice.
Patient characteristics	*Inclusion:* • Neonates who had complete gestational age of 37 weeks and birth weight ≥2500gr and total serum bilirubin level between 18 to 21 mg/dl at the start of phototherapy. • All neonates were exclusively breast-fed.

Bibliographic reference Q2: New	**Author: Babaei (2013)** **Effect of White Plastic Cover around the Phototherapy Unit on Hyperbilirubinemia in Full Term Neonates.** **ID:**
	Exclusion: • Neonates with major congenital anomalies, hemolytic disease, using phenobarbital or herbal medications (such as Alhagi pseudoalhagi, Fumaria parviflora, Zizyphus jujube, Purgative manna and Cichorium Intybus), elevated direct bilirubin (direct bilirubin more than 20% of total serum bilirubin), symptoms of infection and postnatal age less than 48 hours and more than two weeks at the start of phototherapy.
Number of Patients	N = 185 (with cover = 91; without cover = 91) *Baseline characteristics:* Male/female: cover = 32/59; without cover = 32/59 Gestational age (week, mean & SD): cover = 38.2 (0.7); without cover = 38.1 (0.7) Birth weight (g, mean & SD): cover = 3082 (362); without cover = 3182 (386) Age at admission (day, mean & SD): cover = 5.8 (1.9); without cover = 6.2 (2.1) Weight at admission (g, mean & SD): cover = 3054 (351); without cover = 3085 (349) TSB at admission (mg/dL, mean & SD): cover = 19.5 (1.3); without cover = 19.6 (1.1)
Intervention	Standard phototherapy (with white plastic cover around the phototherapy unit) • Continuous standard phototherapy units (model DAVID XHZ2-90) with 6 blue lamps (Philips TL 20W/52, Philips Lighting Co., The Netherlands) were used. • The cover was made of white shiny plastic with thickness of 2 mm, length of 66, width of 36 and height of 45 cm which covered three sides of the unit; one side was uncovered for observing the newborn or performing procedures. The decision to initiation and discontinuation phototherapy was based on 2004 AAP guidelines for management of hyperbilirubinemia in term and near-term newborns.
Comparison	Standard phototherapy (without cover) In both groups, the distance between the infant and the phototherapy lamps was approximately 40 cm.
Length of follow up	Not reported.
Location	Neonatal unit of Imam Reza Hospital, Kermanshah, Iran, from October 2009 to September 2010.
Outcomes measures and	After enrolment, the total serum bilirubin was measured every 12 hours and whenever the serum bilirubin level reached 12.5 mg/dL or was less than that, the infant was discharge from the hospital.

Bibliographic reference Q2: New	**Author: Babaei (2013)** **Effect of White Plastic Cover around the Phototherapy Unit on Hyperbilirubinemia in Full Term Neonates.** **ID:**
effect size	*TSB at 12 hrs after phototherapy (mg/dL, mean & SD):* Cover (n=91) = 16.0 (2.2); without cover (n=91) = 16.9 (2.0), p = 0.009 *TSB at 24 hrs after phototherapy (mg/dL, mean & SD):* Cover (n=86) = 13.7 (2.1); without cover (n=90) = 14.8 (2.3), p = 0.001 *TSB at 36 hrs after phototherapy (mg/dL, mean & SD):* Cover (n=62) = 12.6 (1.9); without cover (n=78) = 13.6 (2.4), p = 0.005 *TSB at 48 hrs after phototherapy (mg/dL, mean & SD):* Cover (n=30) = 12.0 (1.9); without cover (n=52) = 13.3 (2.1), p = 0.003 *Mean duration of phototherapy (hour, mean & SD):* Cover (n=91) = 36.6 (12.9); without cover (n=91) = 50.3 (23.8), p < 0.0001 *Skin rash:* Cover = 18/91; without cover = 16/91, RR = 1.12 (95%CI: 0.61 to 2.06) *Dehydration*: Cover = 0/91; without cover = 0/91, RR = N/A *Hyperthermia:* Cover = 3/91; without cover = 4/91, RR = 0.75 (95%CI: 0.17 to 3.26)
Source of funding	This clinical trial study was registered in IRCT with registration number IRCT201010184961N1.
Comments	Neonates were randomized by sealed, opaque envelopes to control group or covered group. No ITT for some outcomes.

1

Bibliographic reference Q2: New	**Author: Hamid (2013)** **Randomised controlled trial of single phototherapy with reflecting curtains versus double phototherapy in term newborns with hyperbilirubinaemia.** **ID:**
Study type	RCT
Aim	To compare the efficacy of single phototherapy with reflecting curtains (SPRC) and double phototherapy (DP) in treating neonatal jaundice.
Patient characteristics	*Inclusion:* • All jaundiced babies with a birthweight of more than 2.3 kg and requiring intensified phototherapy were eligible for this study.

Bibliographic reference **Q2: New**	**Author: Hamid (2013)** **Randomised controlled trial of single phototherapy with reflecting curtains versus double phototherapy in term newborns with hyperbilirubinaemia.** **ID:**
	• Babies were considered to need intensified phototherapy when they had total serum bilirubin values of more than 300 mmol/L if they were beyond 48 h of age and more 250 mmol/L if they were less than 48 h of age. *Exclusion:* • Babies with serum bilirubin above the exchange transfusion level, congenital abnormalities and presence of direct hyperbilirubinaemia more than 20% and/or presence of infection, as diagnosed by the managing neonatologist.
Number of Patients	N = 156 (SPRC = 78; DP = 78) *Baseline characteristics:* Male/female: SPRC = 50/28; DP = 42/36 Body weight (kg, mean & SD): SPRC = 3.08 (0.44); DP = 3.06 (0.37) Age at start of phototherapy (days, mean & SD): SPRC = 5.12 (2.09); DP = 5.82 (6.85) TSB at start of phototherapy (umol/dL, mean & SD): SPRC = 341.26 (39.80); DP = 347.05 (41.53)
Intervention	Single conventional phototherapy with reflecting curtains (SPRC) • The phototherapy unit used in this study were new Dräger Phototherapy-4000, consisted of four fluorescent tubes special blue light. • The distance between phototherapy unit and the babies was 30 cm. Light intensity was measured from three different angles (front, right and left of infants). The curtains that were made using silver-coloured reflecting cloth, and was hanged from the side of the phototherapy unit, and was approximately 55 cm long. The curtain covered the whole cot except for the foot end part to allow observation of the baby during treatment.
Comparison	Double conventional phototherapy (DP) As above but with double phototherapy units instead.
Length of follow up	Not reported.
Location	Neonatal Intensive Care Unit (NICU), Hospital Universiti Sains Malaysia (HUSM) in Kelantan, Malaysia, from May 2010 to April 2011.
Outcomes measures and	*Serum bilirubin after 4 and 10 h of phototherapy and the duration of required phototherapy were measured.* *6 to 24 hours after stopping phototherapy, another serum bilirubin was checked to look for rebound jaundice (defined as increase in*

Bibliographic reference Q2: New	**Author: Hamid (2013)** **Randomised controlled trial of single phototherapy with reflecting curtains versus double phototherapy in term newborns with hyperbilirubinaemia.** **ID:**
effect size	*serum bilirubin to more than 250 mmol/L).* *Mean (SD) decrease in serum bilirubin after 4 h of phototherapy (umol/dL) (ITT analysis):* SPRC = 22.70 (27.70); DP = 22.53 (28.55), p = 0.97 *Mean (SD) decrease in serum bilirubin after 10 h of phototherapy (umol/dL) (non-ITT analysis):* SPRC = 56.06 (31.36); DP = 58.17 (31.71), p = 0.678 *Mean (SD) TSB at the end of phototherapy (umol/dL) (non-ITT analysis):* SPRC = 218.01 (24.92) DP = 222.87 (21.74), p = 0.196 *Duration of phototherapy (Cox proportional hazard ratio):* Between SPRC and DP: HR = 1.06 (95%CI: 0.88 to 1.27) *Rebound needing restart of phototherapy:* SPRC = 2/78; DP = 2/78, RR = 1.00 (95%CI: 0.14 to 6.92) No other side effects of phototherapy such as hypothermia or hyperthermia, weight loss and others occured during the study.
Source of funding	Funding from the Incentive Grant, Medical School of Universiti Sains Malaysia, Malaysia.
Comments	Block randomisation, based on a computer generated table, was used for the randomisation of all infants into either of two groups. The size of the blocks was variable and not known to the main investigator. Patients were recruited by the main investigator and only after inclusion in the study, consecutively numbered, sealed and opaque envelopes, carrying the allocation, were opened. Lab technicians were blinded.

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Bibliographic reference Q2: New	**Author: Vandborg (2012)** **Dose-Response Relationship of Phototherapy for Hyperbilirubinemia.** **ID:**
Study type	RCT
Aim	To investigate the “saturation point” (ie, an irradiation level above which there is no further decrease in total serum bilirubin [TsB]).
Patient characteristics	*Inclusion:* • Healthy neonates with gestational age ≥33 weeks and uncomplicated hyperbilirubinemia who could receive phototherapy in a bassinet.

Bibliographic reference **Q2: New**	**Author: Vandborg (2012)** **Dose-Response Relationship of Phototherapy for Hyperbilirubinemia.** **ID:**
	Exclusion: • Infants with hemolytic disease due to Rhesus or Kell blood group isoimmunization, or spherocytosis were not included. • Infants who needed double phototherapy or exchange transfusion due to a very high TsB or TsB increasing ≥ 10 umol/L/h were not included. *Indication for phototherapy followed the guidelines of the Danish Pediatric Society, that is, the limit for phototherapy was a TsB (umol/L) corresponding to 10% of the infants' birth weight in grams with maximum TsB of 300 umol/L.*
Number of Patients	N = 151 (at 47cm = 37; at 38cm = 38; at 29cm = 38; at 20cm = 38) *Baseline characteristics (data only available as a single study sample):* Male/female = 86/65 Gestational age (days, median & range) = 254 (231 to 292) Birth weight (g, median & range) = 2780 (1410 to 4500) Age at phototherapy (hour, median & range) = 81 (36 to 486) *TSB at the start of phototherapy (umol/dL, median & 95%CI):* At 47cm = 302 (273 to 347); at 38cm = 288 (274 to 347); at 29cm = 301 (282 to 335); at 20cm = 274 (241 to 301)
Intervention	LED phototherapy at 47cm from the apparatus (to the mattress) *A distance from the phototherapy device to the mattress of 20, 29, 38, or 47 cm measured with a wooden measuring stick corresponded to an average distance between the device and each infant of 12, 21, 30, and 39 cm, respectively.* The phototherapy apparatus used was neoBLUE LED phototherapy device (Natus Medical, San Carlos, CA) emitting blue light with an emission peak at 460 nm and a bandwidth of 450 to 470 nm.
Comparison	LED phototherapy at 38cm, 29cm and 20cm from the apparatus (to the mattress)
Length of follow up	Not reported.
Location	NICU of Aalborg Hospital, Denmark, between July 2009 and December 2010.
Outcomes measures and effect size	*Decrease of TSB from baseline to 24 hours of phototherapy (%, median & 95%CI):* At 47cm = 34% (31% to 38%); at 38cm = 41% (38% to 44%); at 29cm = 40% (36% to 45%); at 20cm = 49% (46% to 53%) *[47cm vs 38cm, p = 0.004]* *[38cm vs 29cm, p = 0.98]*

Bibliographic reference **Q2: New**	**Author: Vandborg (2012)** **Dose-Response Relationship of Phototherapy for Hyperbilirubinemia.** **ID:**
	[29cm vs 20cm, p = 0.001] *Decrease of TSB from baseline to 24 hours of phototherapy (umol/dL, median & 95%CI):* At 47cm = 101 (94 to 115); at 38cm = 117 (105 to 125); at 29cm = 120 (99 to 135); at 20cm = 134 (116 to 142) *TSB after 24 hours of phototherapy (umol/dL, median & 95%CI):* At 47cm = 210 (172 to 235); at 38cm = 167 (154 to 184); at 29cm = 186 (168 to 196); at 20cm = 139 (119 to 159) The only side effects observed were loose stools (but no event rates were reported), no rash was seen.
Source of funding	No external funding.
Comments	The infants were randomized using sealed, opaque envelopes to 1 of 4 phototherapy regimens.

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Appendix H: GRADE profiles

H.1 Review question 1

Table 6: Conventional Phototherapy (ConPT) vs. LED Phototherapy (LED-PT)

Quality assessment							No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Other considerations	ConPT	LED-PT	Mean difference (95% CI)	
Outcome: Mean duration of PT (hours) – Overall term and pre-term infants (less hours better)										
6[1]	RCT	Serious[13]	No serious	No serious	Serious[20]	No serious	205	183	MD = 4.54 (-0.96 to 10.05)	Low
Outcome: Mean duration of PT (hours) – Term infants (less hours better)										
3[2]	RCT	Serious[14]	No serious	No serious	Serious[20]	No serious	122	89	MD = 2.44 (-1.49 to 6.37)	Low
Outcome: Mean duration of PT (hours) – Term infants (less hours better)										
1[3]	RCT	Serious[15]	No serious	Not applicable	Very serious[21]	No serious	20	20	Only median provided: ConPT = 23.0; LED = 30.0, p=0.11	Very low
Outcome: Mean duration of PT (hours) – Pre-term infants (less hours better)										
3[4]	RCT	Serious[16]	No serious	Serious[19]	Serious[20]	No serious	83	94	MD = 8.86 (-3.84 to 21.56)	Very low
Outcome: Mean duration of PT (hours) – Pre-term infants (less hours better)										
1[5]	RCT	Serious[17]	No serious	Not applicable	Very serious[21]	No serious	15	15	ConPT = 108; LED = 110 p>0.05 (no SD provided)	Very low
Outcome: Mean decrease in TSB per hour of PT (umol/L/hour) – Term infants only (higher decrease better)										
3[6]	RCT	Serious[18]	No serious	No serious	No serious	No serious	222	201	MD = -0.07 (-0.54 to 0.39)	Moderate
Outcome: Mean decrease in TSB per hour of PT (umol/L/hour) – Pre-term infants only (higher decrease better)										

Quality assessment							No of patients		Effect estimate		Quality
1[5]	RCT	Serious[17]	No serious	Not applicable	Very serious[21]	No serious	15	15	ConPT = 0.923; LED = 0.975, p>0.05 (no SD provided)		Very low
Outcome: Transepidermal water loss (ml/m^2/hour) – Pre-term infants only (less water loss better)											
1[7]	RCT	Serious[17]	No serious	Not applicable	Serious[20]	No serious	14	17	MD = 6.49 (4.06 to 8.92)		Low
Quality assessment							**No of patients**		**Effect estimate**		**Quality**
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**Other considerations**	**ConPT**	**LED-PT**	**Relative (96% CI)**	**Absolute**	
Outcome: Rebound jaundice - Overall term and pre-term infants											
3[8]	RCT	Serious[18]	No serious	No serious	Very serious[22]	No serious	16/194 (8.2%)	20/206 (9.7%)	0.81 (0.44 to 1.48)	18 fewer per 1000 (from 54 fewer to 47 more)	Very low
Outcome: Rebound jaundice - Term infants											
2[9]	RCT	No serious	No serious	No serious	Very serious[22]	No serious	8/150 (5.3%)	8/162 (4.9%)	1.06 (0.41 to 2.71)	3 more per 1000 (from 29 fewer to 84 more)	Low
Outcome: Rebound jaundice - Pre-term infants											
1[10]	RCT	Serious[17]	No serious	Not applicable	Very serious[22]	No serious	8/44 (18.2%)	12/44 (27.3%)	0.67 (0.30 to 1.47)	90 fewer per 1000 (from 191 fewer to 128 more)	Very low
Outcome: Skin eruption – Pre-term infants only											
1[11]	RCT	Serious[17]	No serious	Not applicable	Very serious[22]	No serious	9/25 (36.0%)	11/33 (33.3%)	1.08 (0.53 to 2.20)	27 more per 1000 (from 157 fewer to 400 more)	Very low
Outcome: Exchange transfusion – Term infants only											
1[12]	RCT	No serious	No serious	Not applicable	Very serious[22]	No serious	0/130 (0%)	2/142 (1.4%)	0.22 (0.01 to	11 fewer per 1000	Low

Quality assessment							No of patients		Effect estimate		Quality
									4.51)	(from 14 fewer to 49 more)	
Outcome: All-cause mortality – Pre-term infants only											
1[11]	RCT	Serious[17]	No serious	Not applicable	Very serious[22]	No serious	1/25 (4.0%)	5/33 (15.2%)	0.26 (0.03 to 2.12)	112 fewer per 1000 (from 147 fewer to 170 more)	Very low

[1] *Demirel (2010); Seidman (2000); Seidman (2003); Bertini (2008); Martins (2007); Surmeli-Onay (2013)*
[2] *Demirel (2010); Seidman (2000); Seidman (2003)*
[3] *Ngerncham (2012)*
[4] *Bertini (2008); Martins (2007); Surmeli-Onay (2013)*
[5] *Viau-Colindres (2012)*
[6] *Kumar (2010); Seidman (2000); Seidman (2003)*
[7] *Bertini (2008)*
[8] *Kumar (2010); Ngerncham (2012); Martins (2007)*
[9] *Kumar (2010); Ngerncham (2012)*
[10] *Martins (2007)*
[11] *Surmeli-Onay (2013)*
[12] *Kumar (2010)*
[13] *Four out of 6 studies did not report randomisation methods; 4 out of 6 studies did not mention allocation concealment, downgrade 1 level.*
[14] *All 3 studies did not report allocation concealment, downgrade 1 level.*
[15] *No report of allocation concealment, downgrade 1 level.*
[16] *All 3 studies did not report methods of randomisation, downgrade 1 level.*
[17] *No report of randomisation method, downgrade 1 level.*
[18] *Two out of 3 studies did not mention allocation concealment, downgrade 1 level.*
[19] *Unexplained significant heterogeneity (I^2>60%), random-effects model was used, downgrade 1 level.*
[20] *Sample size <400, as suggested by the GRADE Working Group for continuous outcomes, downgrade 1 level.*
[21] *Sample size <400, as suggested by the GRADE Working Group for continuous outcomes, no SD or 95%CIs provided, downgrade 2 levels.*
[22] *95%CI crosses over both appreciable benefit and harm – 0.75 and 1.25, downgrade 2 levels.*

Table 7: Conventional PT vs. Fiberoptic PT (Wallaby or Biliblanket)

Quality assessment							No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Other considerations	ConPT	Fiber-PT	Mean difference (95% CI)	
Outcome: Mean duration of PT (hours) – Overall term and pre-term infants (less hours better)										
4[1]	RCT	Serious[13]	No serious	No serious	Serious[20]	No serious	119	151	MD = -2.66	Low

Quality assessment							No of patients		Effect estimate		Quality
									(-13.58 to 8.26)		
Outcome: Mean duration of PT (hours) – Term infants (less hours better)											
1[2]	RCT	Serious[14]	No serious	Not applicable	Serious[20]	No serious	50	50	MD = -11.60 (-17.00 to -6.20)		Low
Outcome: Mean duration of PT (hours) – Pre-term infants (less hours better)											
3[3]	RCT	Serious[15]	No serious	No serious	Serious[20]	No serious	69	101	MD = 3.86 (0.79 to 6.93)		Low
Outcome: Mean decrease in TSB per hour of PT (%) – Term infants only (higher decrease better)											
1[2]	RCT	Serious[14]	No serious	Not applicable	Serious[20]	No serious	50	50	MD = 0.20 (0.08 to 0.32)		Low
Outcome: Mean decrease in TSB from baseline after 48-72hrs PT (%) – Pre-term infants only (higher decrease better)											
1[4]	RCT	Serious[14]	No serious	Not applicable	Serious[20]	No serious	33	70	MD = 0.90 (-1.88 to 3.68)		Low
Outcome: Mean decrease in TSB from baseline after 48hrs PT (umol/L) – Term infants only (higher decrease better)											
1[5]	RCT	Very serious[16]	No serious	Not applicable	Serious[20]	No serious	22	20	MD = 1.70 (-18.61 to 22.01)		Very low
Quality assessment							**No of patients**		**Effect estimate**		**Quality**
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**Other considerations**	**ConPT**	**Fiber-PT**	**Relative (96% CI)**	**Absolute**	
Outcome: Rebound jaundice - Term infants only											
1[2]	RCT	Serious[14]	No serious	Not applicable	Very serious[21]	No serious	3/50 (6.0%)	2/50 (4.0%)	1.50 (0.26 to 8.60)	20 more per 1000 (from 30 fewer to 304 more)	Very low
Outcome: Exchange transfusion – Pre-term infants only											
2[6]	RCT	Serious[17]	No serious	No serious	Very serious[21]	No serious	5/101 (5.0%)	5/124 (4.0%)	1.26 (0.21 to 7.62)	10 more per 1000 (from 32 fewer to 267 more)	Very low
Outcome: Treatment failure (need double PT) – Overall term and pre-term infants											
2[7]	RCT	Serious[18]	No serious	No serious	Very serious[21]	No serious	3/74 (4.1%)	5/70 (7.1%)	0.61 (0.03 to	28 fewer per 1000 (from 69	Very low

Quality assessment							No of patients		Effect estimate		Quality
									13.70)	fewer to 907 more)	
Outcome: Treatment failure (need double PT) – Term infants											
1[2]	RCT	Serious[14]	No serious	Not applicable	Very serious[21]	No serious	0/50 (0%)	4/50 (8.0%)	0.11 (0.01 to 2.01)	71 fewer per 1000 (from 79 fewer to 81 more)	Very low
Outcome: Treatment failure (need double PT) – Pre-term infants											
1[8]	RCT	Serious[19]	No serious	Not applicable	Very serious[21]	No serious	3/24 (12.5%)	1/20 (5.0%)	2.50 (0.28 to 22.20)	75 more per 1000 (from 36 fewer to 1000 more)	Very low
Outcome: Erythema - Overall term and pre-term infants											
2[9]	RCT	Serious[17]	No serious	No serious	Very serious[21]	No serious	11/83 (13.3%)	18/120 (15.0%)	1.23 (0.65 to 2.35)	35 more per 1000 (from 53 fewer to 203 more)	Very low
Outcome: Erythema - Term infants											
1[2]	RCT	Serious[14]	No serious	Not applicable	Very serious[21]	No serious	1/50	1/50	1.00 (0.06 to 15.55)	0 fewer per 1000 (19 fewer to 291 more)	Very low
Outcome: Erythema - Pre-term infants											
1[4]	RCT	Serious[14]	No serious	Not applicable	Very serious[21]	No serious	10/33 (30.3%)	17/70 (24.3%)	1.25 (0.64 to 2.42)	61 more per 1000 (from 87 fewer to 345 more)	Very low
Outcome: All-cause mortality – Pre-term infants only											
1[10]	RCT	Serious[14]	No serious	Not applicable	Very serious[21]	No serious	2/68 (2.9%)	2/56 (3.6%)	0.82 (0.12 to 5.66)	6 fewer per 1000 (from 31 fewer to 166 more)	Very low
Outcome: No. of infants with watery stools – Term infants only											
1[2]	RCT	Serious[14]	No serious	Not applicable	Very serious[21]	No serious	3/50 (6.0%)	3/50 (6.0%)	1.00 (0.21 to 4.72)	0 fewer per 1000 (from 47 fewer to 223 more)	Very low

Quality assessment							No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Other considerations	ConPT	Fiber-PT	Mean difference (95% CI)	
Outcome: Skin temperature after 24-36hrs PT (°C) – Pre-term infants only (lower better)										
1[11]	RCT	Serious[14]	No serious	Not applicable	Serious[20]	No serious	12	11	MD = -0.20 (-0.45 to 0.05)	Low
Outcome: Skin temperature during PT (forehead) (°C) – Term infants only (lower better)										
1[12]	RCT	Serious[14]	No serious	Not applicable	Serious[20]	No serious	21	20	MD = 0.47 (0.12 to 0.82)	Low
Outcome: Skin temperature during PT (abdomen) (°C) – Term infants only (lower better)										
1[12]	RCT	Serious[14]	No serious	Not applicable	Serious[20]	No serious	21	20	MD = 0.47 (0.16 to 0.78)	Low
Outcome: Skin temperature during PT (left leg) (°C) – Term infants only (lower better)										
1[12]	RCT	Serious[14]	No serious	Not applicable	Serious[20]	No serious	21	20	MD = 0.03 (-0.34 to 0.40)	Low
Outcome: Skin temperature during PT (back) (°C) – Term infants only (lower better)										
1[12]	RCT	Serious[14]	No serious	Not applicable	Serious[20]	No serious	21	20	MD = 0.08 (-0.23 to 0.39)	Low

[1] *Sarici (2001); Costello (1995); Dani (2004); Romagnoli (2006)*
[2] *Sarici (2001)*
[3] *Costello (1995); Dani (2004); Romagnoli (2006)*
[4] *Romagnoli (2006)*
[5] *Gale (1990)*
[6] *Romagnoli (2006); Van Kaam (1998)*
[7] *Sarici (2001); Costello (1995)*
[8] *Costello (1995)*
[9] *Sarici (2001); Romagnoli (2006)*
[10] *Van Kaam (1998)*
[11] *Dani (2004)*
[12] *Pezzati (2002)*
[13] *Three out of 4 studies did not report randomisation methods, downgrade 1 level.*
[14] *Did not report method of randomisation, downgrade 1 level.*
[15] *Two out of 3 studies did not report randomisation methods, downgrade 1 level.*
[16] *Did not report method of randomisation nor allocation concealment, downgrade 2 level.*
[17] *Both studies did not report method of randomisation, downgrade 1 level.*
[18] *One study did not report method of randomisation, the other no mention of allocation concealment, downgrade 1 level.*
[19] *Did not mention allocation concealment, downgrade 1 level.*
[20] *Sample size <400, as suggested by the GRADE Working Group for continuous outcomes, downgrade 1 level.*

[21] *95%CI crosses over both appreciable benefit and harm – 0.75 and 1.25, downgrade 2 levels.*

Table 8: Conventional PT vs. Conventional PT + Fiberoptic PT

Quality assessment							No of patients		Effect estimate		Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Other considerations	ConPT	ConPT + Fiber-PT	Mean difference (95% CI)		
Outcome: Mean decrease in TSB from baseline after 18hrs PT (umol/L) – Pre-term infants only (more decrease better)											
1[1]	RCT	Serious[3]	No serious	Not applicable	Serious[5]	No serious	37	33	MD = -22.23 (-32.26 to -12.20)		Low
Outcome: Mean decrease in TSB from baseline after 18hrs PT (%) – Pre-term infants only (more decrease better)											
1[1]	RCT	Serious[3]	No serious	Not applicable	Serious[5]	No serious	37	33	MD = -15.00 (-21.12 to -8.88)		Low
Outcome: Mean decrease in TSB from baseline after 48-72hrs PT (%) – Pre-term infants only (more decrease better)											
1[2]	RCT	Serious[4]	No serious	Not applicable	Serious[5]	No serious	33	33	MD = -8.40 (-11.78 to -5.02)		Low
Outcome: Mean duration of PT (hours) – Pre-term infants only (less hours better)											
1[2]	RCT	Serious[4]	No serious	Not applicable	Serious[5]		33	33	MD = 15.10 (3.54 to 26.66)		Low
Quality assessment							**No of patients**		**Effect estimate**		**Quality**
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**Other considerations**	**ConPT**	**ConPT + Fiber-PT**	**Relative (96% CI)**	**Absolute**	
Outcome: Rebound jaundice – Pre-term infants only											
1[1]	RCT	Serious[3]	No serious	Not applicable	Very serious[6]	No serious	14/37 (37.8%)	12/33 (36.4%)	1.04 (0.56 to 1.92)	15 more per 1000 (from 160 fewer to 335 more)	Very low
Outcome: Exchange transfusion – Pre-term infants only											
1[2]	RCT	Serious[4]	No serious	Not applicable	Very serious[6]	No serious	2/33 (6.1%)	0/33 (0%)	5.00 (0.25 to 100.32)	1000 more per 1000 (from 273 fewer to 1000 more)	Very low
Outcome: Erythema – Pre-term infants only											
1[2]	RCT	Serious[4]	No serious	Not applicable	Very serious[6]	No serious	10/33	12/33	0.83 (0.42 to	62 fewer per 1000 (from 211	Very low

Quality assessment							No of patients		Effect estimate		Quality
							(30.3%)	(36.4%)	1.66)	fewer to 240 more)	

[1] *Holtrop (1992)*
[2] *Romagnoli (2006)*
[3] *Did not report allocation concealment, downgrade 1 level.*
[4] *Did not report method of randomisation, downgrade 1 level.*
[5] *Sample size <400, as suggested by the GRADE Working Group for continuous outcomes, downgrade 1 level.*
[6] *95%CI crosses over both appreciable benefit and harm – 0.75 and 1.25, downgrade 2 levels.*

H.2 Review question 2

Table 9: Conventional PT – Blue light vs. Conventional – Turquoise light

Quality assessment							No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Other considerations	ConPT-Blue	ConPT-Turuoise	Mean difference (95% CI)	
Outcome: Mean decrease in TSB from baseline after 24hrs PT (umol/L) – Pre-term infants only (more decrease better)										
1[1]	RCT	Serious[2]	No serious	Not applicable	Serious[3]	No serious	69	72	MD = -14.00 (-24.24 to -3.76)	Low

[1] *Ebbesen (2007)*
[2] *Did not report method of randomisation, downgrade 1 level.*
[3] *Sample size <400, as suggested by the GRADE Working Group for continuous outcomes, downgrade 1 level.*

Table 10: Conventional PT – Blue light vs. Conventional – Green light

Quality assessment							No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Other considerations	ConPT-Blue	ConPT-Green	Mean difference (95% CI)	
Outcome: Mean duration of PT (hours) – Overall term and pre-term infants (lower better)										
4[1]	RCT	Serious[8]	No serious	No serious	Serious[14]	No serious	187	188	MD = -5.04 (-13.55 to 3.47)	Low
Outcome: Mean duration of PT (hours) – Term infants only (lower better)										
3[2]	RCT	Serious[9]	No serious	Serious[13]	Serious[14]	No serious	87	88	MD = -11.28 (-25.06 to 2.49)	Low
Outcome: Mean duration of PT (hours) – Pre-term infants only (lower better)										
1[3]	RCT	Very	No serious	Not	Serious[14]	No serious	100	100	MD = 7.20	Very low

Quality assessment							No of patients		Effect estimate	Quality
		serious[10]		applicable					(6.40 to 8.00)	
Outcome: Mean decrease in TSB per hour of PT (umol/L/hour) - Overall term and pre-term infants (more decrease better)										
3[4]	RCT	Serious[9]	No serious	No serious	Serious[14]	No serious	172	173	MD = -0.41 (-0.46 to -0.36)	Low
Outcome: Mean decrease in TSB per hour of PT (umol/L/hour) - Term infants (more decrease better)										
2[5]	RCT	Serious[11]	No serious	No serious	Serious[14]	No serious	72	73	MD = -0.38 (-0.52 to -0.24)	Low
Outcome: Mean decrease in TSB per hour of PT (umol/L/hour) - Pre-term infants (more decrease better)										
1[3]	RCT	Very serious[10]	No serious	Not applicable	Serious[14]	No serious	100	100	MD = -0.41 (-0.46 to -0.36)	Very low
Outcome: Mean decrease in TSB from baseline after 24hrs PT (umol/L) – Term infants only (more decrease better)										
1[6]	RCT	Serious[12]	No serious	Not applicable	Serious[14]	No serious	15	15	MD = 43.40 (23.67 to 63.13)	Low
Outcome: Mean decrease in TSB from baseline after 72hrs PT (%) – Pre-term infants only (more decrease better)										
1[7]	RCT	Very serious[10]	No serious	Not applicable	Serious[14]	No serious	20	20	MD = 17.30 (15.52 to 19.08)	Very low

Quality assessment							No of patients		Effect estimate		Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Other considerations	ConPT-Blue	ConPT-Green	Relative (96% CI)	Absolute	
Outcome: Rebound jaundice - Term infants only											
1[6]	RCT	Serious[12]	No serious	Not applicable	No serious	No serious	12/15 (80.0%)	3/15 (20.0%)	4.00 (1.41 to 11.35)	600 more per 1000 (from 82 more to 1000 more)	Moderate

[1] *Amato (1991); Ayyash (1987); Ayyash (1987b); Ayyash (1987a)*
[2] *Amato (1991); Ayyash (1987); Ayyash (1987b)*
[3] *Ayyash (1987a)*
[4] *Ayyash (1987); Ayyash (1987b); Ayyash (1987a)*
[5] *Ayyash (1987); Ayyash (1987b)*
[6] *Amato (1991)*
[7] *Romagnoli (1988)*
[8] *All 4 studies did not report allocation concealment, downgrade 1 level.*
[9] *All 3 studies did not report allocation concealment, downgrade 1 level.*
[10] *Did not report randomisation method nor allocation concealment, downgrade 2 levels.*

[11] *Both studies did not report allocation concealment, downgrade 1 level.*
[12] *Did not report allocation concealment, downgrade 1 level.*
[13] *Unexplained significant heterogeneity (I2>60%), random-effects model was used, downgrade 1 level.*
[14] *Sample size <400, as suggested by the GRADE Working Group for continuous outcomes, downgrade 1 level.*

Table 11: Conventional PT – Supine vs. Conventional PT – Changing

Quality assessment							No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Other considerations	ConPT-Supine	ConPT-Changing	Mean difference (95% CI)	
Outcome: Mean duration of PT (hours) – Term infants (lower better)										
3[1]	RCT	Serious[5]	No serious	Serious[8]	Serious[9]	No serious	94	87	MD = -3.06 (-10.92 to 4.80)	Very low
Outcome: Mean decrease in TSB per hour of PT (umol/L/hour) – Term infant only (more decrease better)										
2[2]	RCT	No serious	No serious	No serious	Serious[9]	No serious	78	73	MD = -0.13 (-0.54 to 0.28)	Moderate
Outcome: Mean decrease in TSB from baseline after 24hrs PT (%) – Term infants only (more decrease better)										
2[3]	RCT	Serious[6]	No serious	Serious[8]	Serious[9]	No serious	40	41	MD = 2.81 (-6.99 to 12.60)	Very low
Outcome: Mean decrease in TSB from baseline after 24hrs PT (umol/L) – Term infants only (more decrease better)										
1[4]	RCT	Serious[7]	No serious	Not applicable	Serious[9]	No serious	16	14	MD = 23.94 (-0.59 to 48.47)	Low

[1] *Bhethanabhotla (2013); Chen (2002); Shinwell (2002)*
[2] *Bhethanabhotla (2013); Chen (2002)*
[3] *Chen (2002); Shinwell (2002)*
[4] *Shinwell (2002)*
[5] *Two out of 3 studies did not report method of randomisation, downgrade 1 level.*
[6] *Both studies did not report method of randomisation, downgrade 1 level.*
[7] *Did not report method of randomisation, downgrade 1 level.*
[8] *Unexplained significant heterogeneity (I^2>60%), random-effects model was used, downgrade 1 level.*
[9] *Sample size <400, as suggested by the GRADE Working Group for continuous outcomes, downgrade 1 level.*

Table 12: Conventional PT vs. Conventional PT + Curtains

Quality assessment							No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Other considerations	ConPT	ConPT + Curtains	Mean difference (95% CI)	
Outcome: Mean duration of PT (hours) – Term infants only (less better)										

Quality assessment							No of patients		Effect estimate		Quality
2[1]	RCT	Serious[6]	No serious	Serious[9]	Serious[10]	No serious	133	133	MD = 7.71 (-4.14 to 19.57)		Very low
Outcome: Mean decrease in TSB from baseline after 24hrs PT (%) – Term infants only (more decrease better)											
2[2]	RCT	Serious[6]	No serious	No serious	Serious[10]	No serious	76	78	MD = -7.64 (-11.51 to -3.78)		Low
Outcome: Mean decrease in TSB from baseline after 4hrs PT (umol/L) – Term infants only (more decrease better)											
1[3]	RCT	Very serious[7]	No serious	Not applicable	Serious[10]	No serious	49	51	MD = -23.58 (-33.28 to -13.88)		Very low
Outcome: Mean decrease in TSB from baseline after 8hrs PT (umol/L) – Term infants only (more decrease better)											
1[4]	RCT	Seriuos[8]	No serious	Not applicable	Serious[10]	No serious	42	42	MD = -3.42 (-5.96 to -0.88)		Low
Quality assessment							**No of patients**		**Effect estimate**		**Quality**
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**Other considerations**	**ConPT**	**ConPT + Curtains**	**Relative (96% CI)**	**Absolute**	
Outcome: Skin rash – Term infants only											
1[5]	RCT	Seriuos[8]	No serious	Not applicable	Serious[11]	No serious	16/91 (17.6%)	8/91 (8.8%)	2.00 (0.90 to 4.44)	88 more per 1000 (from 9 fewer to 302 more)	Low
Outcome: Hyperthemia – Term infants only											
1[5]	RCT	Seriuos[8]	No serious	Not applicable	Very serious[12]	No serious	4/91 (4.4%)	3/91 (3.3%)	1.33 (0.31 to 5.79)	11 more per 1000 (from 23 fewer to 158 more)	Very low

[1] *Babaei (2013); Sivanandan (2009)*
[2] *Eggert (1988); Sivanandan (2009)*
[3] *Djokomuljanto (2006)*
[4] *Sivanandan (2009)*
[5] *Babaei (2013)*
[6] *Both studies did not report method of randomisation, downgrade 1 level.*
[7] *Did not report both method of randomisation nor allocation concealment, downgrade 2 levels.*
[8] *Did not report method of randomisation, downgrade 1 level.*
[9] *Unexplained significant heterogeneity (I^2>60%), random-effects model was used, downgrade 1 level.*
[10] *Sample size <400, as suggested by the GRADE Working Group for continuous outcomes, downgrade 1 level.*
[11] *95%CI crosses over1.25, downgrade 1 level.*

[12] *95%CI crosses over both appreciable benefit and harm – 0.75 and 1.25, downgrade 2 levels.*

Table 13: Double Conventional PT vs. Conventional PT + Curtains

Quality assessment							No of patients		Effect estimate		Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Other considerations	Double ConPT	ConPT+ Curtains	Mean difference (95% CI)		
Outcome: Mean decrease in TSB from baseline after 4hrs PT (umol/L) – Term infants only (more decrease better)											
1[1]	RCT	No serious	No serious	Not applicable	Serious[2]	No serious	78	78	MD = -0.17 (-9.00 to 8.66)		Moderate
Quality assessment							**No of patients**		**Effect estimate**		**Quality**
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**Other considerations**	**Double ConPT**	**ConPT+ Curtains**	**Relative (96% CI)**	**Absolute**	
Outcome: Rebound jaundice – Term infants only											
1[1]	RCT	No serious	No serious	Not applicable	Very serious[3]	No serious	2/78 (2.6%)	2/78 (2.6%)	1.00 (0.14 to 6.92)	0 fewer per 1000 (from 22 fewer to 152 more)	Low

[1] *Hamid (2013)*
[2] *Sample size <400, as suggested by the GRADE Working Group for continuous outcomes, downgrade 1 level.*
[3] *95%CI crosses over both appreciable benefit and harm – 0.75 and 1.25, downgrade 2 levels.*

Table 14: Conventional PT + Feeds vs. Conventional PT + Feeds + Extra fluids

Quality assessment							No of patients		Effect estimate		Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Other considerations	ConPT + Feeds	ConPT + Feeds + Extra fluids	Mean difference (95% CI)		
Outcome: Mean duration of PT (hours) – Term infants only (less better)											
1[1]	RCT	No serious	No serious	Not applicable	Serious[2]	No serious	37	37	MD = 21.00 (9.45 to 32.55)		Moderate
Outcome: Mean decrease in TSB from baseline after 24hrs PT (%) – Term infants only (more decrease better)											
1[1]	RCT	No serious	No serious	Not applicable	Serious[2]	No serious	37	37	MD = -8.00 (-13.25 to -2.75)		Moderate
Quality assessment							**No of patients**		**Effect estimate**		**Quality**
No of	**Design**	**Risk of**	**Indirectness**	**Inconsistency**	**Imprecision**	**Other**	**ConPT +**	**ConPT + Feeds +**	**Relative**	**Absolute**	

Quality assessment							No of patients		Effect estimate		Quality
studies		bias				considerations	Feeds	Extra fluids	(96% CI)		
Outcome: Exchange transfusion – Term infants only											
1[1]	RCT	No serious	No serious	Not applicable	Serious[3]	No serious	20/37 (54.1%)	6/37 (16.2%)	3.33 (1.51 to 7.35)	378 more per 1000 (from 83 more to 1000 more)	Moderate

[1] *Mehta (2005)*
[2] *Sample size <400, as suggested by the GRADE Working Group for continuous outcomes, downgrade 1 level.*
[3] *Very small sample size.*

Table 15: Conventional PT + Enteral feeds vs. Conventional PT + 50% Enteral & 50% IV feeds

Quality assessment							No of patients		Effect estimate		Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Other considerations	ConPT + enteral feeds	ConPT + 50%enteral & 50%IV feeds	Mean difference (95% CI)		
Outcome: Mean decrease in iSB per hour of PT (umol/L/hour) – Term infants only (more decrease better)											
1[1]	RCT	No serious	No serious	Not applicable	Serious[2]	No serious	27	27	MD = -0.80 (-4.15 to 2.55)		Moderate
Quality assessment							**No of patients**		**Effect estimate**		**Quality**
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**Other considerations**	**ConPT + enteral feeds**	**ConPT + 50%enteral & 50%IV feeds**	**Relative (96% CI)**	**Absolute**	
Outcome: Exchange transfusion – Term infants only											
1[1]	RCT	No serious	No serious	Not applicable	Very serious[3]	No serious	5/27 (18.5%)	8/27 (29.6%)	0.63 (0.23 to 1.67)	110 fewer per 1000 (from 228 fewer to 199 more)	Low

[1] *Boo (2002)*
[2] *Sample size <400, as suggested by the GRADE Working Group for continuous outcomes, downgrade 1 level.*
[3] *95%CI crosses over both appreciable benefit and harm – 0.75 and 1.25, downgrade 2 levels.*

Table 16: Conventional PT – Breastfeeding vs. Conventional PT – Formula feeds

Quality assessment	No of patients	Effect estimate	Quality

Quality assessment							No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Other considerations	ConPT - Breastfeeding	ConPT – Formula feeds	Mean difference (95% CI)	
Outcome: Mean decrease in TSB from baseline after 24hrs PT (umol/L) – Term infants only (more decrease better)										
1[1]	RCT	Serious[2]	No serious	Not applicable	Serious[3]	No serious	38	36	MD = 12.00 (-5.13 to 29.13)	Low

[1] *Martinez (1993)*
[2] *Did not report allocation concealment, downgrade 1 level.*
[3] *Sample size <400, as suggested by the GRADE Working Group for continuous outcomes, downgrade 1 level.*

Table 17: Continuous Conventional PT vs Intermittent Conventional PT (4 hrs on, 4 hrs off)

Quality assessment							No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Other considerations	Continuous ConPT	4h on 4h off	Mean difference (95% CI)	
Outcome: Mean duration of PT (hour) – Term infants only (less better)										
1[1]	RCT	Very serious[2]	No serious	Not applicable	Serious[3]	No serious	13	9	MD = 3.20 (-31.79 to 38.19	Very low
Outcome: Mean decrease in TSB per hour of PT (umol/L/hour) – Term infants only (more decrease better)										
1[1]	RCT	Very serious[2]	No serious	Not applicable	Serious[3]	No serious	13	9	MD = -0.41 (-2.71 to 1.89)	Very low

[1] *Lau (1984)*
[2] *Did not report method of randomisation nor allocation concealment, downgrade 2 levels.*
[3] *Sample size <400, as suggested by the GRADE Working Group for continuous outcomes, downgrade 1 level.*

Table 18: Continuous Conventional PT vs Intermittent Conventional PT (1 hr on, 3 hrs off)

Quality assessment							No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Other considerations	Continuous ConPT	1hr on 3 hr off	Mean difference (95% CI)	
Outcome: Mean duration of PT (hour) – Term infants only (less better)										
1[1]	RCT	Very serious[2]	No serious	Not applicable	Serious[3]	No serious	13	12	MD = -10.10 (-55.48 to 35.28)	Very low
Outcome: Mean decrease in TSB per hour of PT (umol/L/hour) – Term infants only (more decrease better)										

Quality assessment							No of patients		Effect estimate	Quality
1[1]	RCT	Very serious[2]	No serious	Not applicable	Serious[3]	No serious	13	12	MD = -0.01 (-2.42 to 4.42)	Very low

[1] *Lau (1984)*
[2] *Did not report method of randomisation nor allocation concealment, downgrade 2 levels.*
[3] *Sample size <400, as suggested by the GRADE Working Group for continuous outcomes, downgrade 1 level.*

Table 19: LED PT – Blue vs. LED PT – Blue-Green

Quality assessment							No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Other considerations	LED-PT - Supine	LED-PT - Changing	Mean difference (95% CI)	
Outcome: Mean duration of PT – Term infants only (less better)										
1[1]	RCT	Serious[2]	No serious	Not applicable	Serious[3]	No serious	25	22	MD = -7.60 (-20.74 to 5.54)	Low
Outcome: Mean decrease in TSB per hour of PT (umol/L) – Term infants only (more decrease better)										
1[1]	RCT	Serious[2]	No serious	Not applicable	Serious[3]	No serious	53	59	MD = 1.27 (-0.49 to 3.03)	Low

[1] *Holtrop (1992)*
[2] *Did not mention allocation concealment, downgrade 1 level.*
[3] *Sample size <400, as suggested by the GRADE Working Group for continuous outcomes, downgrade 1 level.*

Table 20: LED PT – Supine vs. LED PT – Changing

Quality assessment							No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Other considerations	LED-PT - Supine	LED-PT - Changing	Mean difference (95% CI)	
Outcome: Mean decrease in TSB from baseline after 24hrs PT (%) – Term infants only (more decrease better)										
1[1]	RCT	Serious[2]	No serious	Not applicable	Serious[3]	No serious	53	59	MD = 1.00 (-2.42 to 4.42)	Low

[1] *Donneborg (2010)*
[2] *Did not report method of randomisation, downgrade 1 level.*
[3] *Sample size <400, as suggested by the GRADE Working Group for continuous outcomes, downgrade 1 level.*

Table 21: LED PT – Distance from mattress – 47cm vs 38cm vs 29cm vs 20cm

Quality assessment							No of patients		Effect estimate	Quality
No of	Design	Risk of	Indirectness	Inconsistency	Imprecision	Other	LED-P	LED-PT 38cm	Median difference	

Quality assessment							No of patients		Effect estimate	Quality
studies		bias				considerations	47cm	29cm 20cm		
Outcome: Mean decrease in TSB from baseline after 24hrs PT (umol/L) – Term infants only (more decrease better)										
1[1]	RCT	Serious[2]	No serious	Not applicable	Very serious[3]	No serious	37	38cm = 38 29cm = 38 20cm = 38	Only median reported: 47cm = 101 38cm = 117 29cm = 120 20cm = 134 (47cm vs 38cm, p=0.004) (38cm vs 29cm, p=0.98) (29cm vs 20cm, p=0.001)	Very low

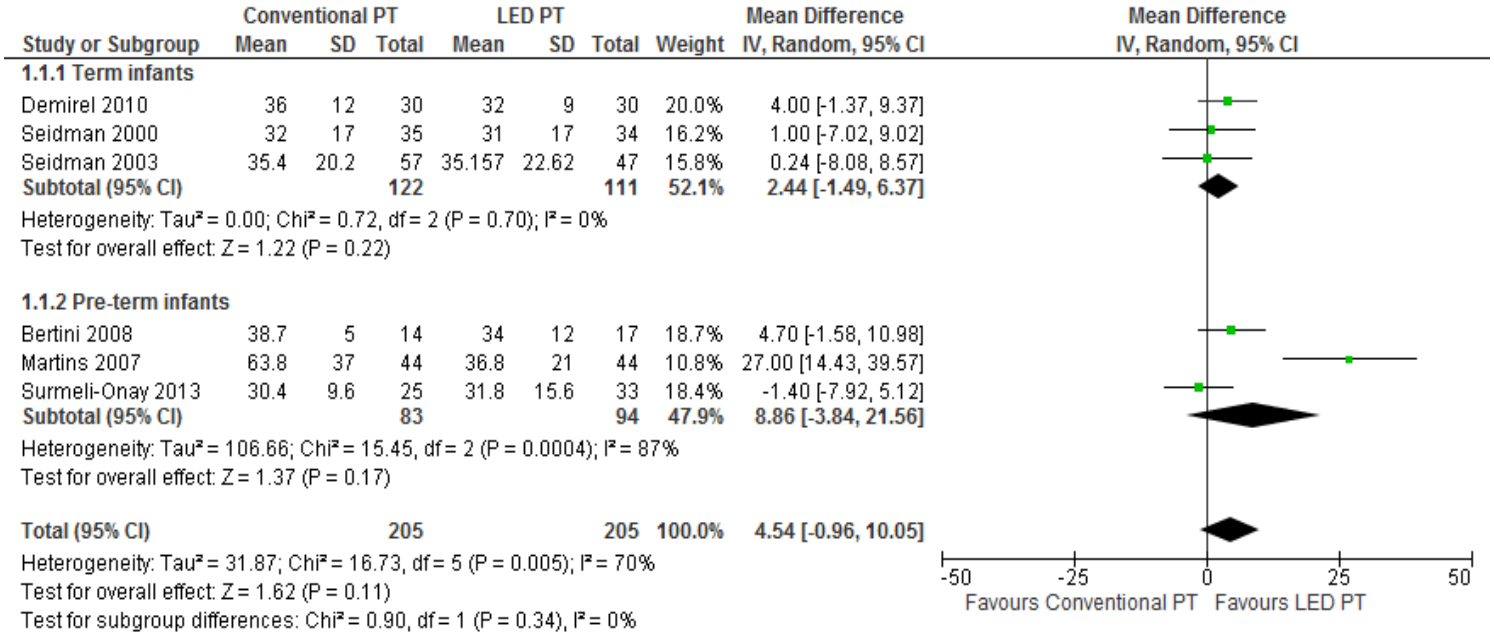
1 [1] *Vandborg (2012)*
2 [2] *Did not report method of randomisation, downgrade 1 level.*
3 [3] *Very small sample size, only median was reported with no SD nor 95%CI, downgrade 2 levels.*

Appendix I: Forest plots

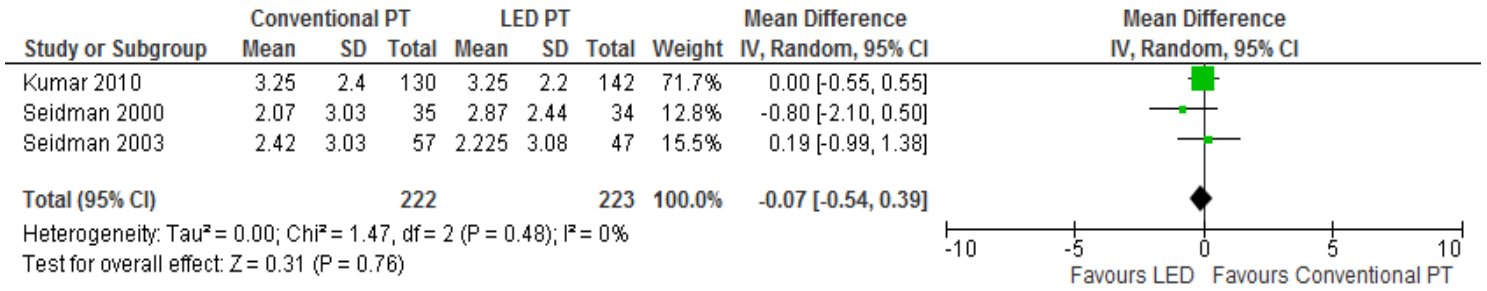
I.1 Review question 1

I.1.1 Conventional PT vs. LED PT

Conventional PT vs. LED PT: Mean duration of PT (hours)

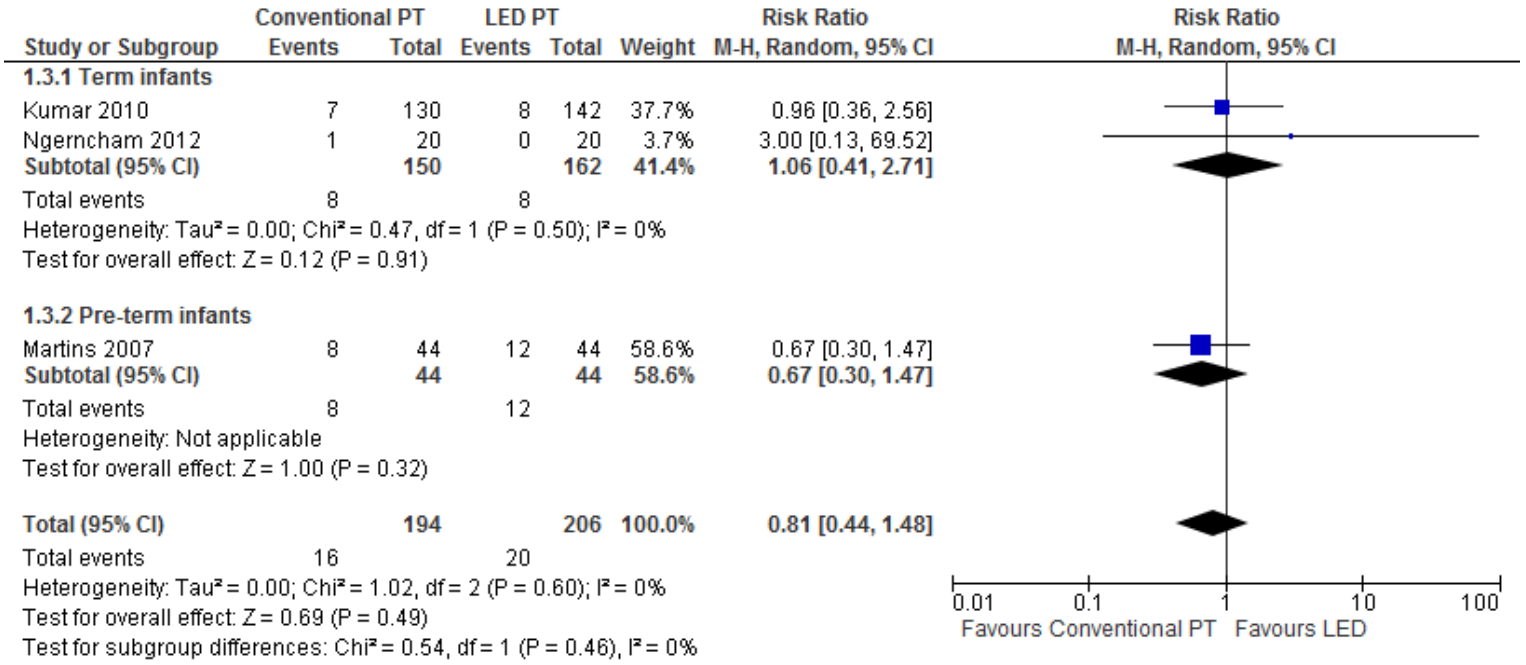


1 **Conventional PT vs. LED PT: Mean decrease in TSB per hour (umol/L/hour) – Term only**



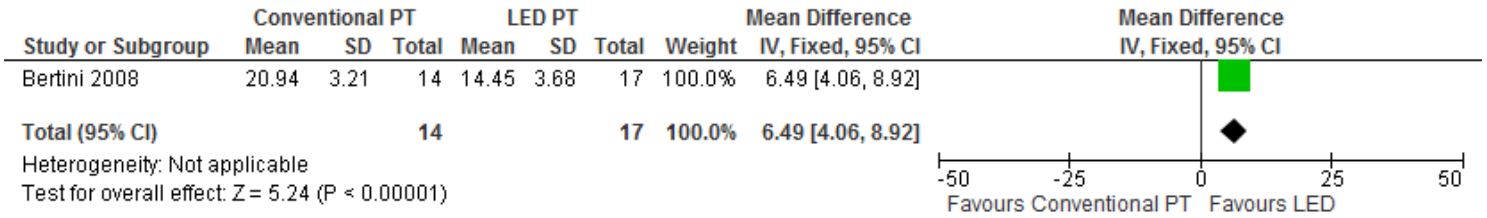
2

3 **Conventional PT vs. LED PT: Rebound jaundice**



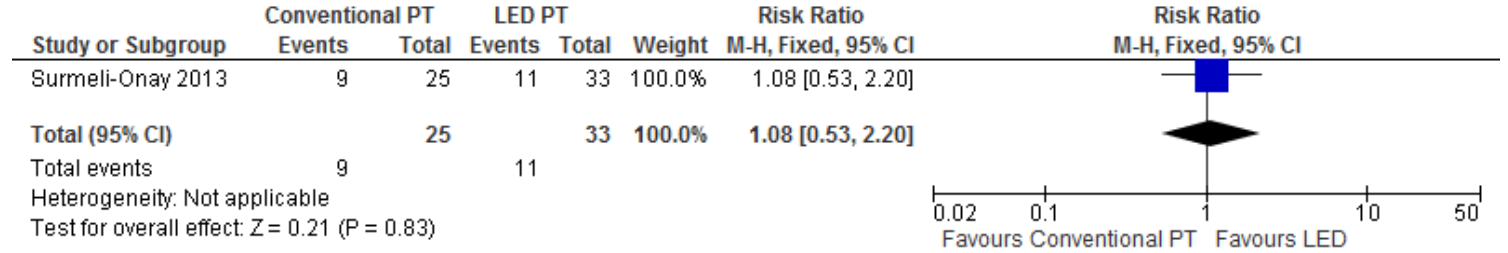
4

1 **Conventional PT vs. LED PT: Transepidermal water loss (ml/m2/hour) – Pre-term only**



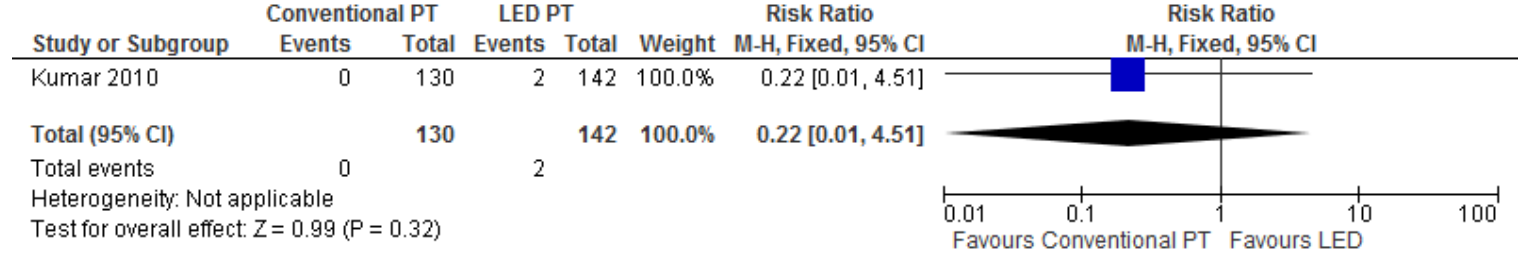
2

3 **Conventional PT vs. LED PT: Skin eruption – Pre-term only**



4

5 **Conventional PT vs. LED PT: Exchange transfusion – Term only**

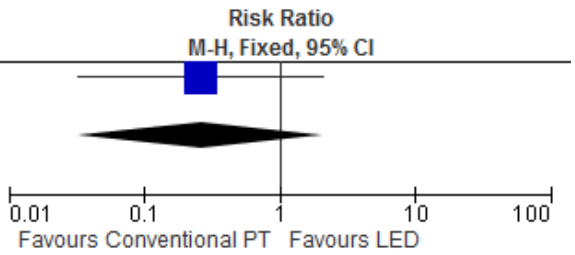


6

Conventional PT vs. LED PT: All-cause mortality – Pre-term only

Study or Subgroup	Conventional PT Events	Conventional PT Total	LED PT Events	LED PT Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Surmeli-Onay 2013	1	25	5	33	100.0%	0.26 [0.03, 2.12]
Total (95% CI)		**25**		**33**	**100.0%**	**0.26 [0.03, 2.12]**
Total events	1		5			

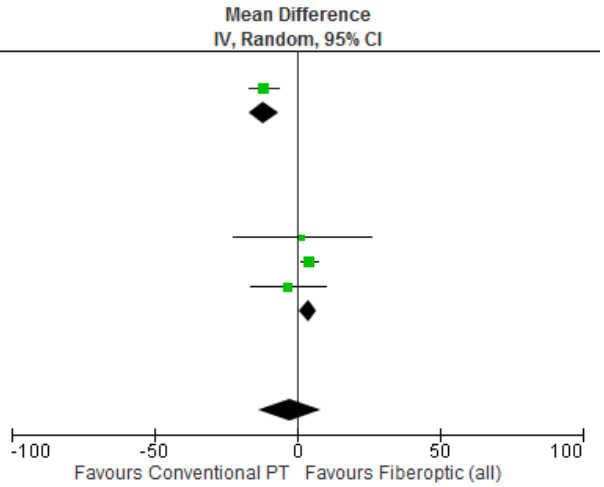
Heterogeneity: Not applicable
Test for overall effect: Z = 1.25 (P = 0.21)



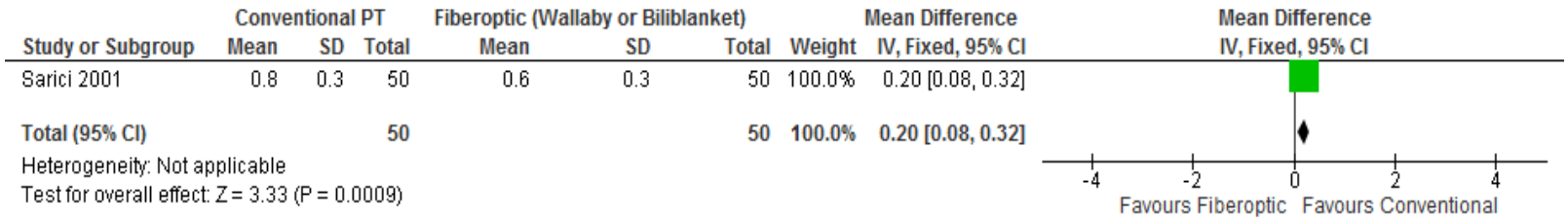
I.1.2 Conventional PT vs. Fiberoptic PT (Wallaby or Biliblanket)

Conventional PT vs. Fiberoptic PT: Mean duration of PT (hours)

Study or Subgroup	Conventional PT Mean	Conventional PT SD	Conventional PT Total	Fiberoptic (Wallaby or Biliblanket) Mean	Fiberoptic (Wallaby or Biliblanket) SD	Fiberoptic (Wallaby or Biliblanket) Total	Weight	Mean Difference IV, Random, 95% CI
1.1.1 Term infants								
Sarici 2001	49.4	14.4	50	61	13.1	50	31.4%	-11.60 [-17.00, -6.20]
Subtotal (95% CI)			**50**			**50**	**31.4%**	**-11.60 [-17.00, -6.20]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.21 (P < 0.0001)								
1.1.2 Pre-term infants								
Costello 1995	44	42.8	24	42	39.1	20	12.7%	2.00 [-22.22, 26.22]
Dani 2004	43	3.1	12	38.7	4.5	11	33.0%	4.30 [1.11, 7.49]
Romagnoli(c) 2006	90.2	24.3	33	93.25	43	70	22.9%	-3.05 [-16.10, 10.00]
Subtotal (95% CI)			**69**			**101**	**68.6%**	**3.86 [0.79, 6.93]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.17$, df = 2 (P = 0.56); $I^2 = 0\%$								
Test for overall effect: Z = 2.46 (P = 0.01)								
Total (95% CI)			**119**			**151**	**100.0%**	**-2.66 [-13.58, 8.26]**
Heterogeneity: $Tau^2 = 91.32$; $Chi^2 = 24.99$, df = 3 (P < 0.0001); $I^2 = 88\%$								
Test for overall effect: Z = 0.48 (P = 0.63)								
Test for subgroup differences: $Chi^2 = 23.81$, df = 1 (P < 0.00001), $I^2 = 95.8\%$								

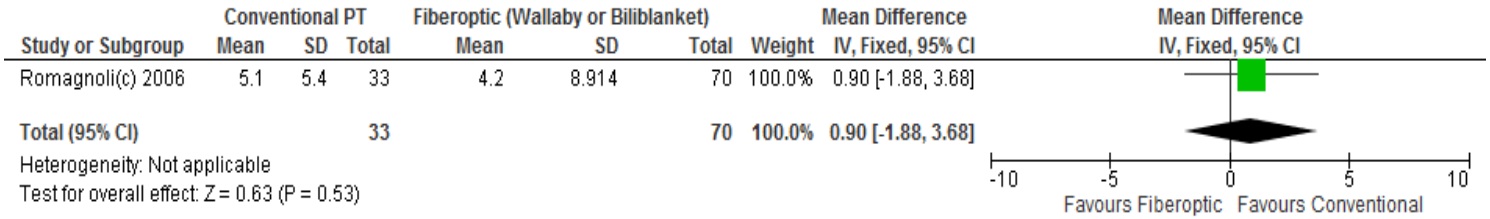


1 **Conventional PT vs. Fiberoptic PT: Mean decrease in TSB per hour during PT (% per hour) – Term only**



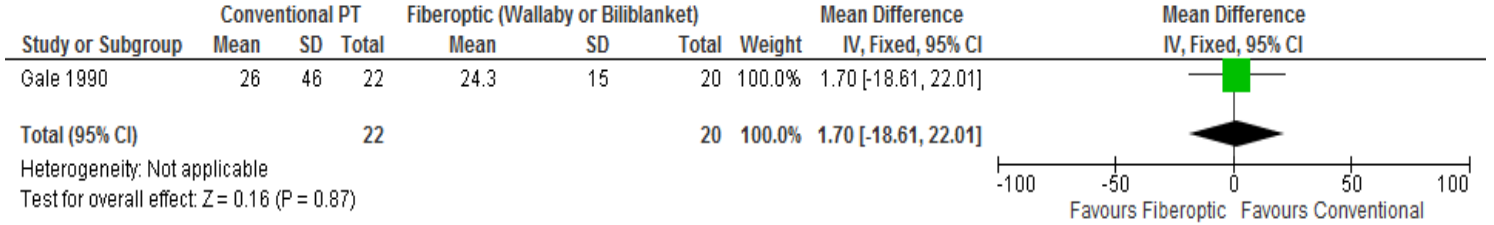
2

3 **Conventional PT vs. Fiberoptic PT: Mean decrease in TSB from baseline after 48-72hrs PT (%) – Pre-term only**



4

5 **Conventional PT vs. Fiberoptic PT: Mean decrease in TSB from baseline after 48hrs PT (umol/L) – Term only**

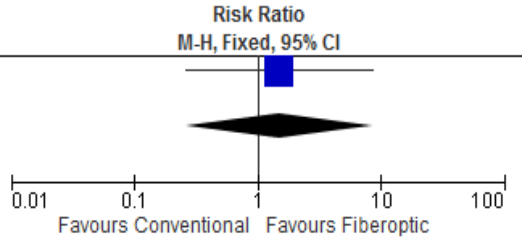


6

Conventional PT vs. Fiberoptic PT: Rebound jaundice – Term only

Study or Subgroup	Conventional PT Events	Conventional PT Total	Fiberoptic (Wallaby or Biliblanket) Events	Fiberoptic (Wallaby or Biliblanket) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Sarici 2001	3	50	2	50	100.0%	1.50 [0.26, 8.60]
Total (95% CI)		**50**		**50**	**100.0%**	**1.50 [0.26, 8.60]**
Total events	3		2			

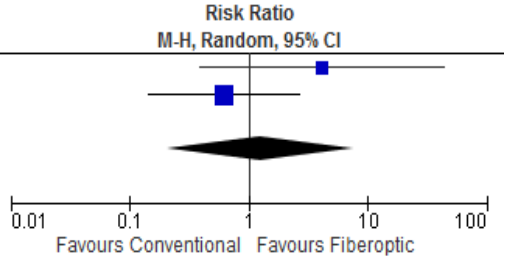
Heterogeneity: Not applicable
Test for overall effect: Z = 0.46 (P = 0.65)



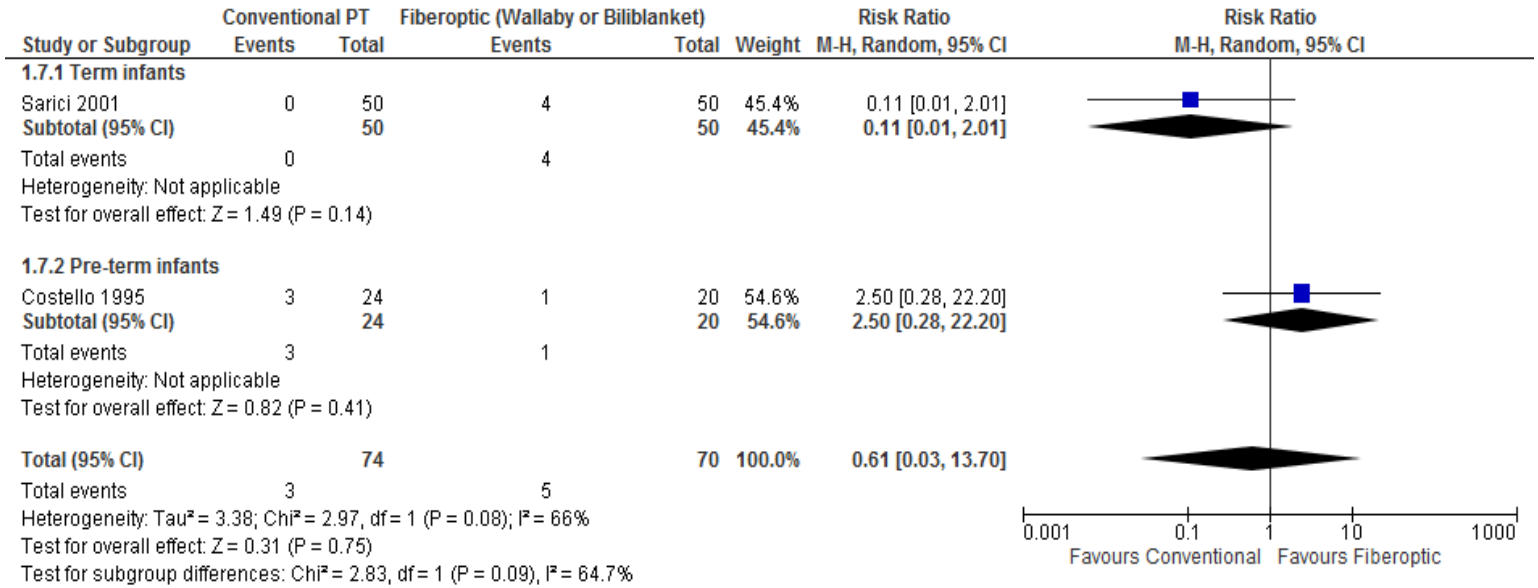
Conventional PT vs. Fiberoptic PT: Exchange transfusion – Pre-term only

Study or Subgroup	Conventional PT Events	Conventional PT Total	Fiberoptic (Wallaby or Biliblanket) Events	Fiberoptic (Wallaby or Biliblanket) Total	Weight	Risk Ratio M-H, Random, 95% CI
Romagnoli(c) 2006	2	33	1	68	37.5%	4.12 [0.39, 43.83]
Van Kaam 1998	3	68	4	56	62.5%	0.62 [0.14, 2.65]
Total (95% CI)		**101**		**124**	**100.0%**	**1.26 [0.21, 7.62]**
Total events	5		5			

Heterogeneity: Tau² = 0.80; Chi² = 1.80, df = 1 (P = 0.18); I² = 44%
Test for overall effect: Z = 0.25 (P = 0.80)

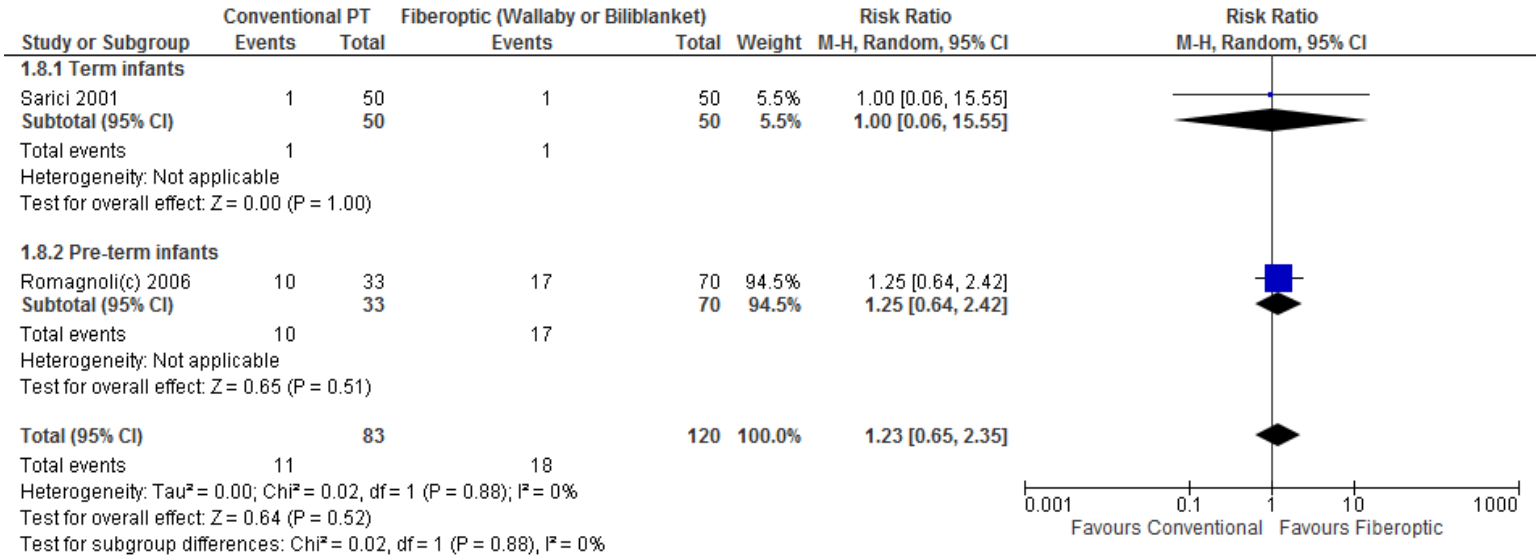


1 Conventional PT vs. Fiberoptic PT: Treatment failure (need double PT)

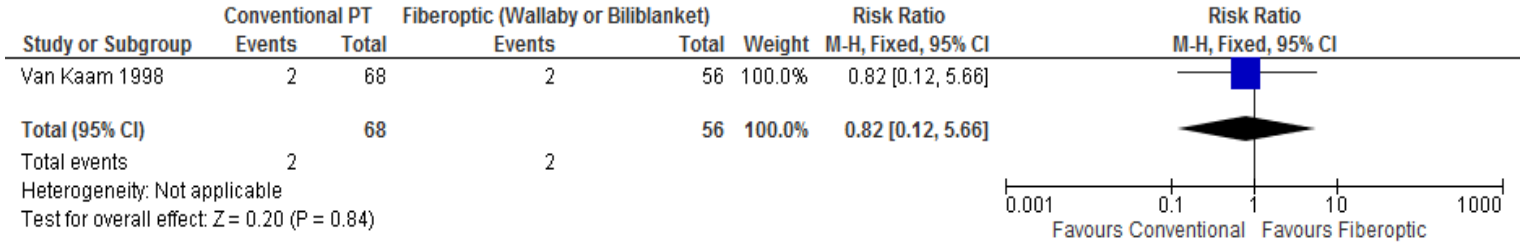


2

Conventional PT vs. Fiberoptic PT: Erythema



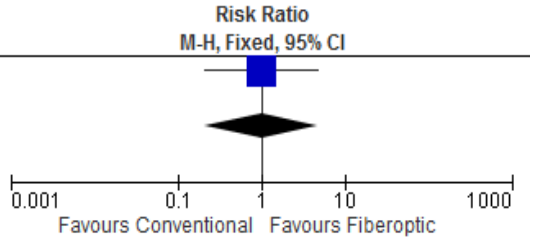
Conventional PT vs. Fiberoptic PT: All-cause mortality – Pre-term only



1 **Conventional PT vs. Fiberoptic PT: No. of infants with watery stools – Term only**

Study or Subgroup	Conventional PT Events	Conventional PT Total	Fiberoptic (Wallaby or Biliblanket) Events	Fiberoptic (Wallaby or Biliblanket) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Sarici 2001	3	50	3	50	100.0%	1.00 [0.21, 4.72]
Total (95% CI)		**50**		**50**	**100.0%**	**1.00 [0.21, 4.72]**
Total events	3		3			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)

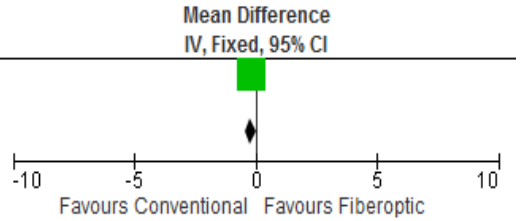


2

3 **Conventional PT vs. Fiberoptic PT: Skin temperature after 24-36hrs PT (°C) – Pre-term only**

Study or Subgroup	Conventional PT Mean	Conventional PT SD	Conventional PT Total	Fiberoptic (Wallaby or Biliblanket) Mean	Fiberoptic (Wallaby or Biliblanket) SD	Fiberoptic (Wallaby or Biliblanket) Total	Weight	Mean Difference IV, Fixed, 95% CI
Dani 2004	36.4	0.3	12	36.6	0.3	11	100.0%	-0.20 [-0.45, 0.05]
Total (95% CI)			**12**			**11**	**100.0%**	**-0.20 [-0.45, 0.05]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.60 (P = 0.11)

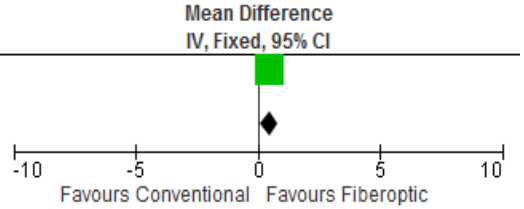


4

5 **Conventional PT vs. Fiberoptic PT: Skin temperature during PT (forehead) (°C) – Term only**

Study or Subgroup	Conventional PT Mean	Conventional PT SD	Conventional PT Total	Fiberoptic (Wallaby or Biliblanket) Mean	Fiberoptic (Wallaby or Biliblanket) SD	Fiberoptic (Wallaby or Biliblanket) Total	Weight	Mean Difference IV, Fixed, 95% CI
Pezzati 2002	36.74	0.7	21	36.27	0.4	20	100.0%	0.47 [0.12, 0.82]
Total (95% CI)			**21**			**20**	**100.0%**	**0.47 [0.12, 0.82]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.66 (P = 0.008)

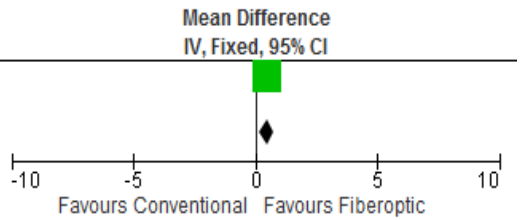


6

1 **Conventional PT vs. Fiberoptic PT: Skin temperature during PT (abdomen) (°C) – Term only**

Study or Subgroup	Conventional PT Mean	SD	Total	Fiberoptic (Wallaby or Biliblanket) Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Pezzati 2002	36.99	0.6	21	36.52	0.4	20	100.0%	0.47 [0.16, 0.78]
Total (95% CI)			**21**			**20**	**100.0%**	**0.47 [0.16, 0.78]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.96 (P = 0.003)

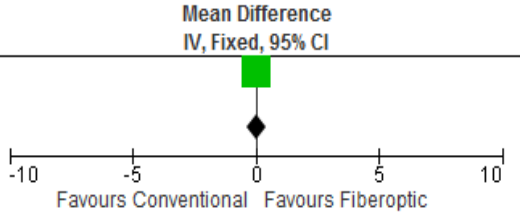


2

3 **Conventional PT vs. Fiberoptic PT: Skin temperature during PT (left leg) (°C) – Term only**

Study or Subgroup	Conventional PT Mean	SD	Total	Fiberoptic (Wallaby or Biliblanket) Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Pezzati 2002	36.41	0.8	21	36.38	0.3	20	100.0%	0.03 [-0.34, 0.40]
Total (95% CI)			**21**			**20**	**100.0%**	**0.03 [-0.34, 0.40]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.16 (P = 0.87)

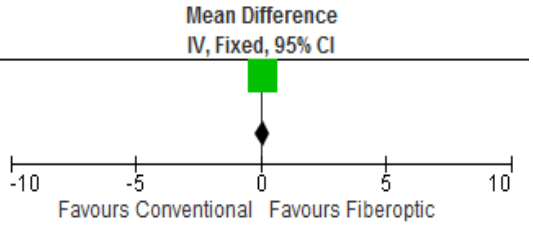


4

5 **Conventional PT vs. Fiberoptic PT: Skin temperature during PT (back) (°C) – Term only**

Study or Subgroup	Conventional PT Mean	SD	Total	Fiberoptic (Wallaby or Biliblanket) Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Pezzati 2002	36.7	0.6	21	36.62	0.4	20	100.0%	0.08 [-0.23, 0.39]
Total (95% CI)			**21**			**20**	**100.0%**	**0.08 [-0.23, 0.39]**

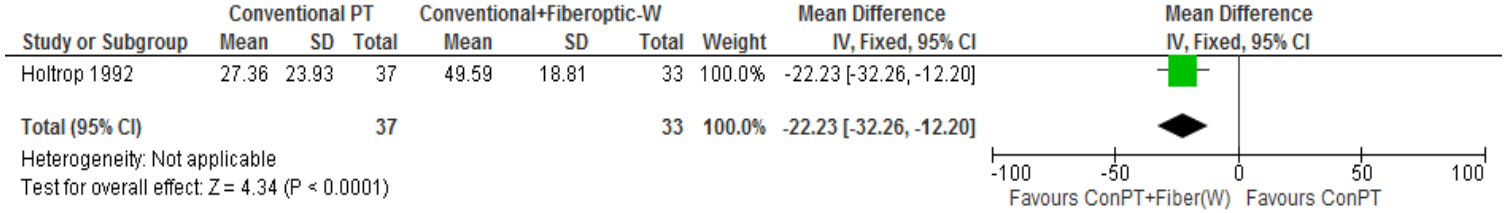
Heterogeneity: Not applicable
Test for overall effect: Z = 0.50 (P = 0.61)



6

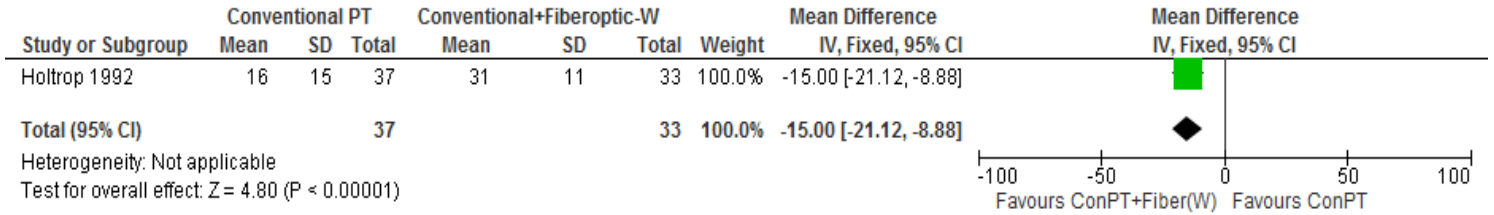
I.1.31 Conventional PT vs. Conventional + Fiberoptic PT

2 Conventional PT vs. Conventional + Fiberoptic PT: Mean decrease in TSB from baseline after 18hrs PT (umol/L) – Pre-erm only



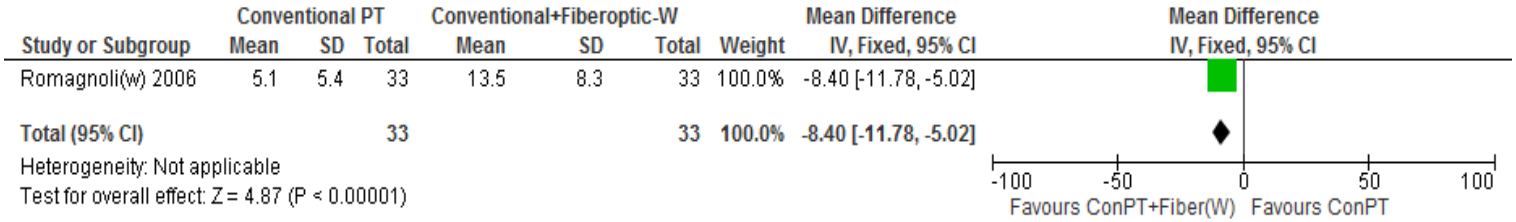
3

4 Conventional PT vs. Conventional + Fiberoptic PT: Mean decrease in TSB from baseline after 18hrs PT (%) – Pre-term only



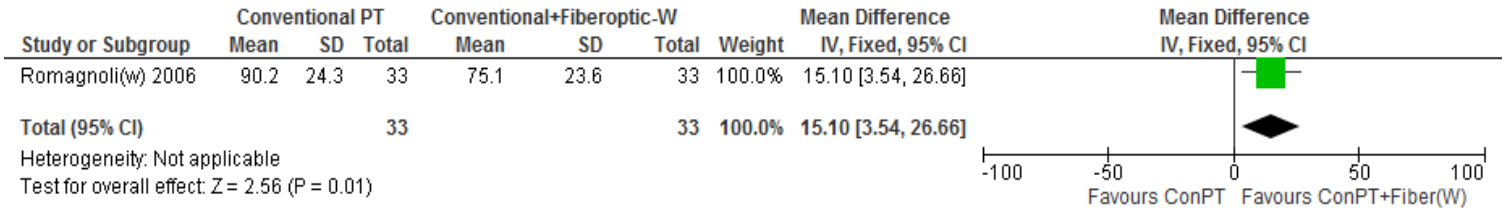
5

6 Conventional PT vs. Conventional + Fiberoptic PT: Mean decrease in TSB from baseline after 48-72hrs PT (%) – Pre-term only



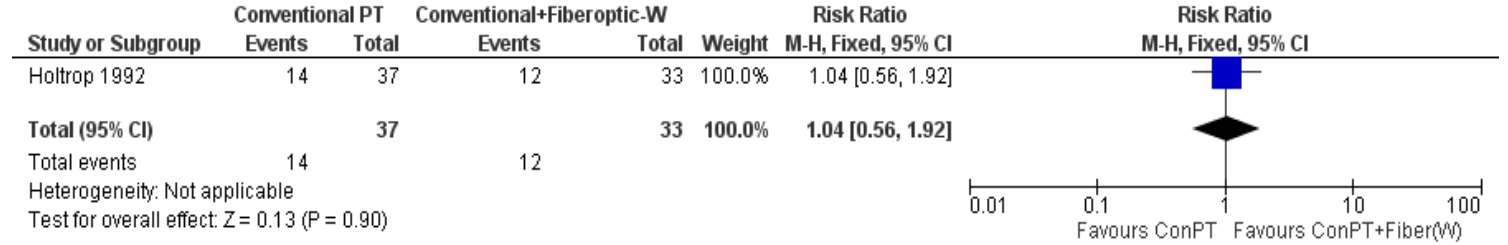
7

1 **Conventional PT vs. Conventional + Fiberoptic PT: Mean duration of PT (hours) – Pre-term only**



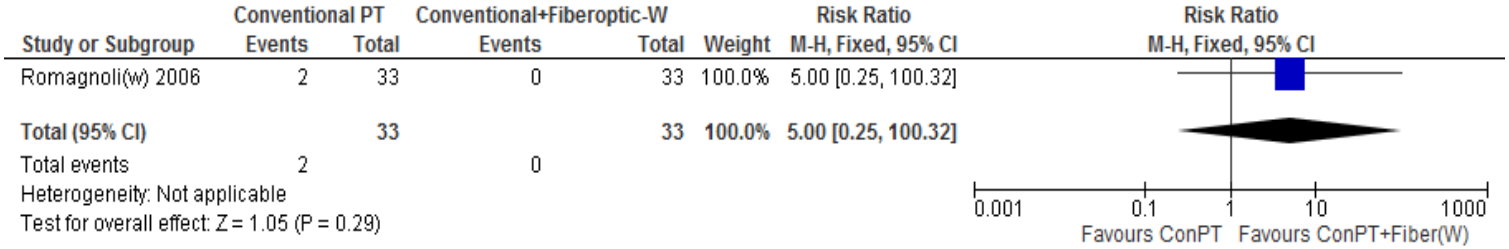
2

3 **Conventional PT vs. Conventional + Fiberoptic PT: Rebound jaundice – Pre-term only**



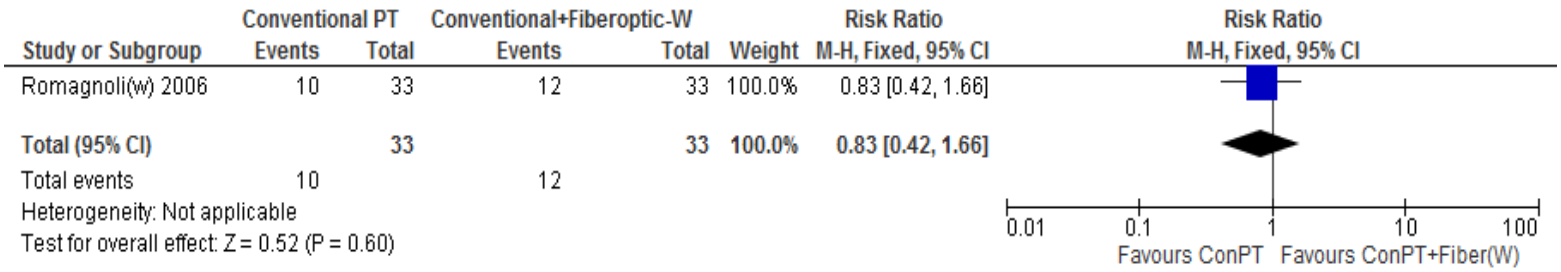
4

5 **Conventional PT vs. Conventional + Fiberoptic PT: Exchange transfusion – Pre-term only**



6

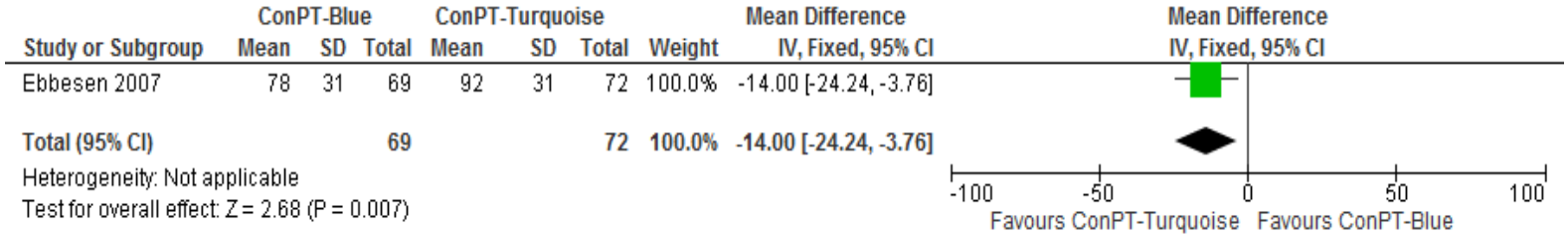
Conventional PT vs. Conventional + Fiberoptic PT: Erythema – Pre-term only



I.2 Review question 2

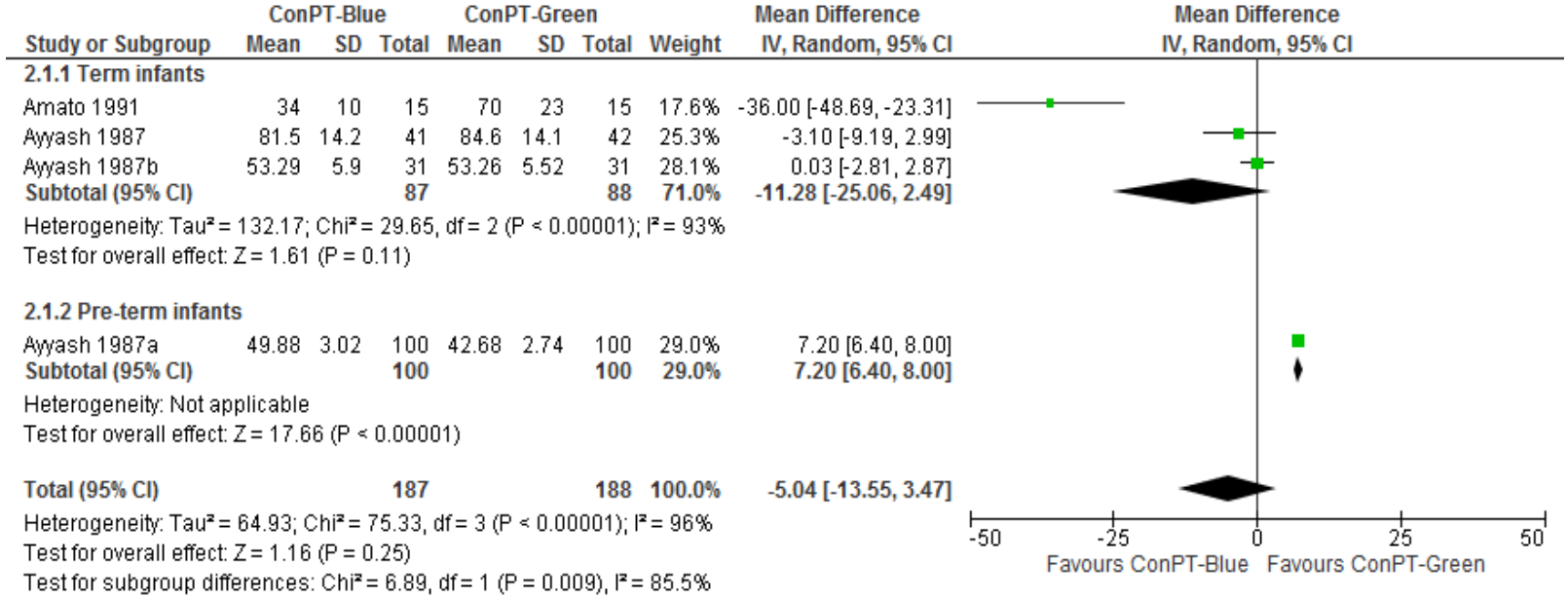
I.2.1 Conventional PT – Blue light vs. Conventional – Turquoise light

Conventional PT – Blue light vs. Conventional – Turquoise light: Mean decrease in TSB from baseline after 24hrs PT (umol/L) – Pre-term only



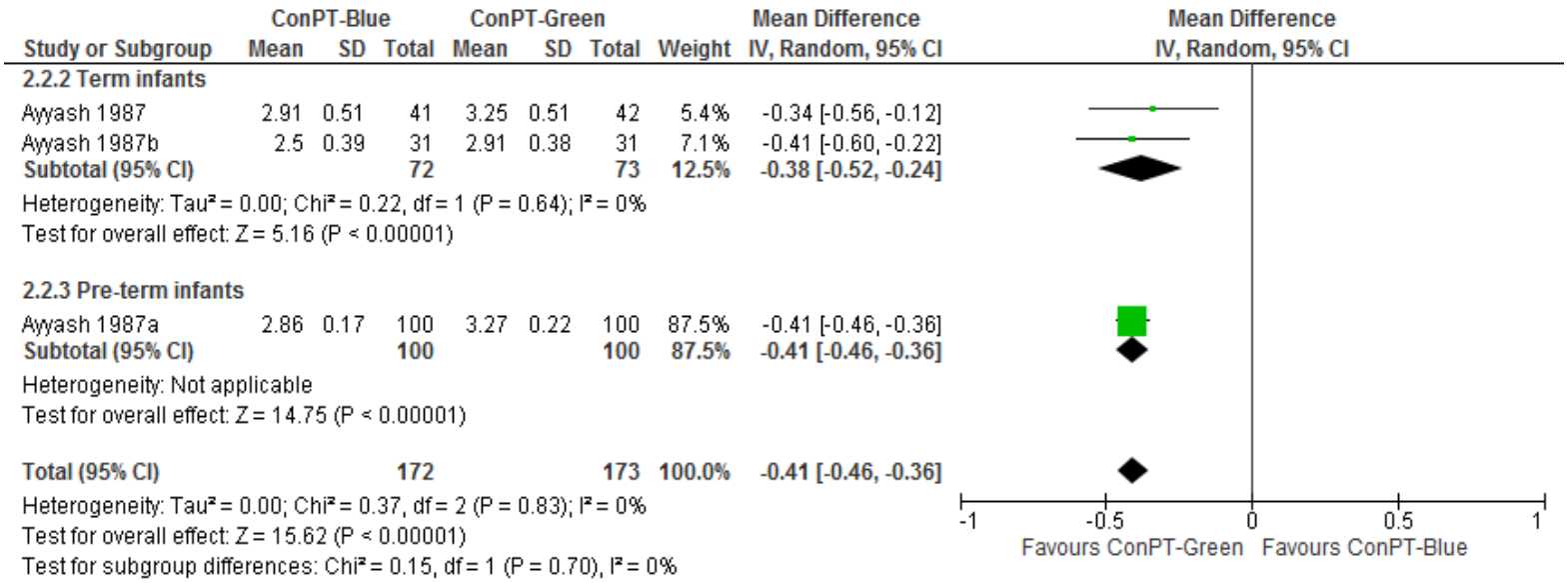
I.2.21 Conventional PT – Blue light vs. Conventional – Green light

2 Conventional PT – Blue light vs. Conventional – Green light: Mean duration of PT (hours)



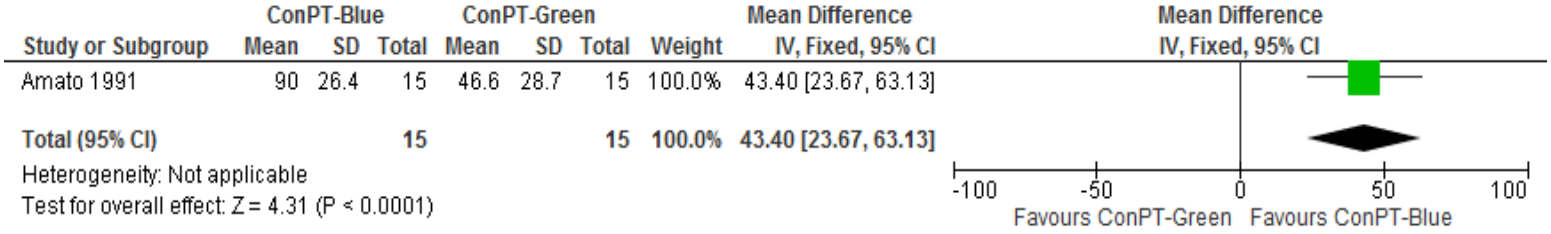
3

1 **Conventional PT – Blue light vs. Conventional – Green light: Mean decrease in TSB per hour of PT (umol/L/hour)**



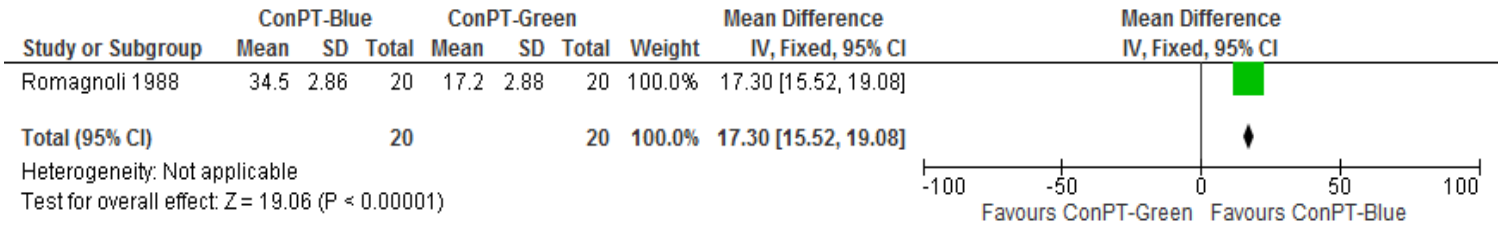
2

3 **Conventional PT – Blue light vs. Conventional – Green light: Mean decrease in TSB from baseline after 24hrs PT (umol/L) – Term only**

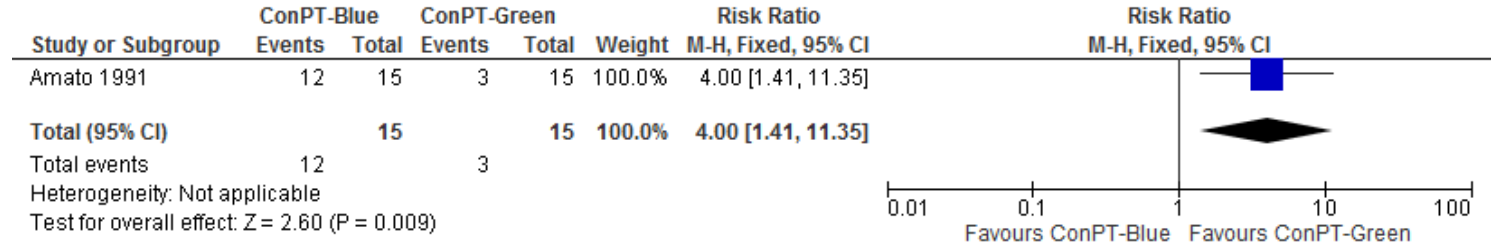


4

Conventional PT – Blue light vs. Conventional – Green light: Mean decrease in TSB from baseline after 72hrs PT (%) – Pre-term only

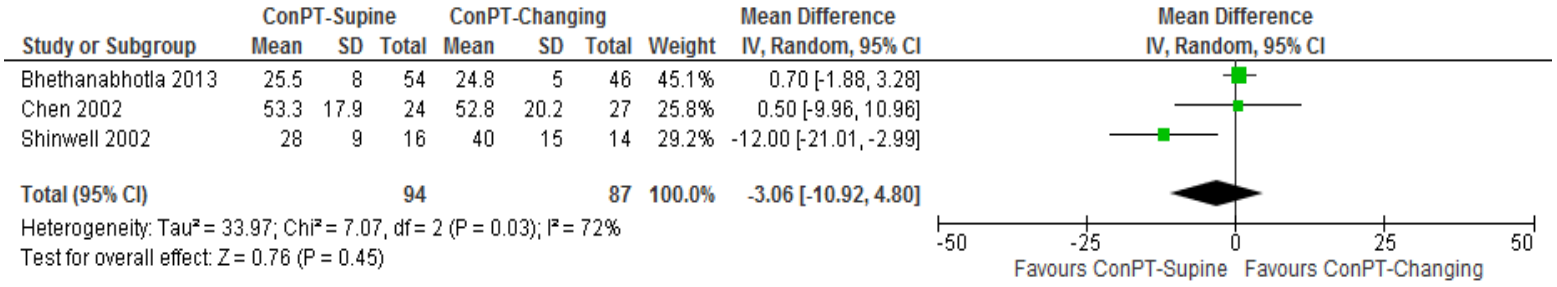


Conventional PT – Blue light vs. Conventional – Green light: Rebound jaundice – Term only

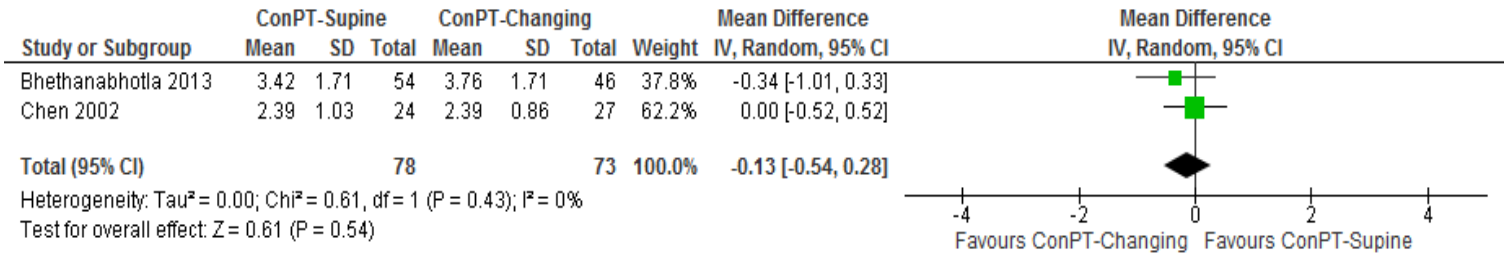


I.2.3 Conventional PT – Supine vs. Conventional PT – Changing

Conventional PT – Supine vs. Conventional PT – Changing: Mean duration of PT (hours) – Term only

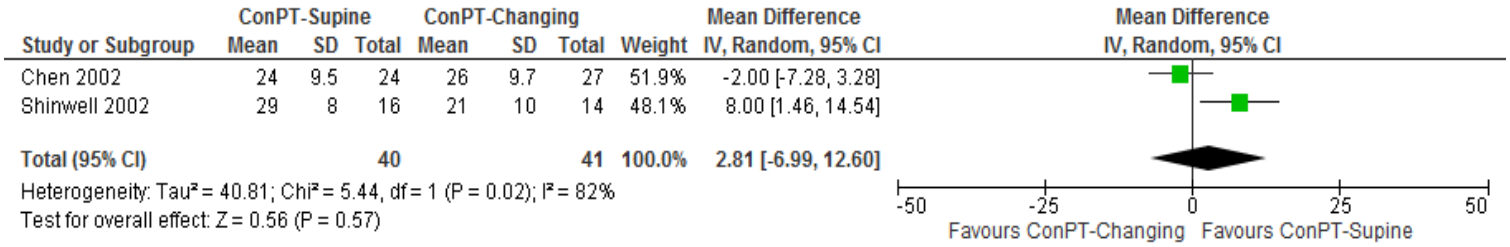


1 **Conventional PT – Supine vs. Conventional PT – Changing: Mean decrease in TSB per hour of PT (umol/L/hour) – Term only**



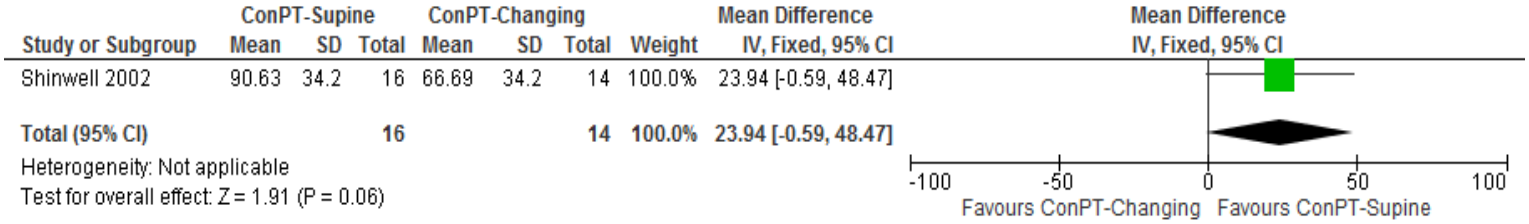
2

3 **Conventional PT – Supine vs. Conventional PT – Changing: Mean decrease in TSB from baseline after 24hrs PT (%) – Term only**



4

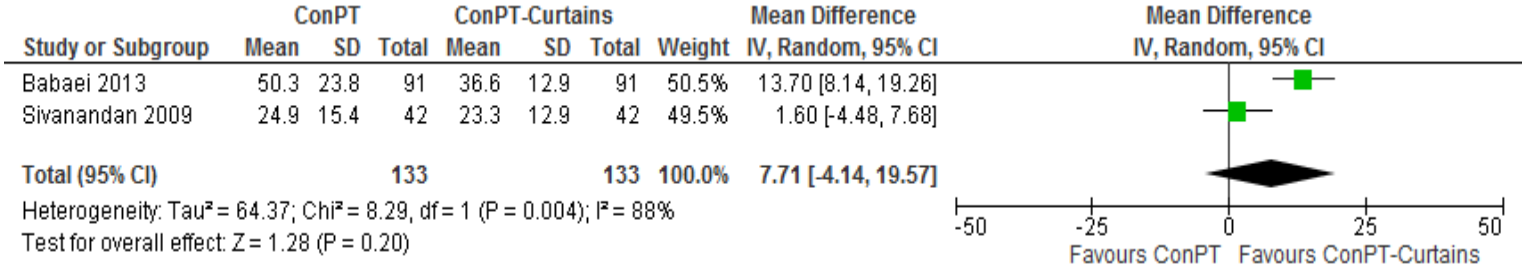
5 **Conventional PT – Supine vs. Conventional PT – Changing: Mean decrease in TSB from baseline after 24hrs PT (umol/L) – Term only**



6

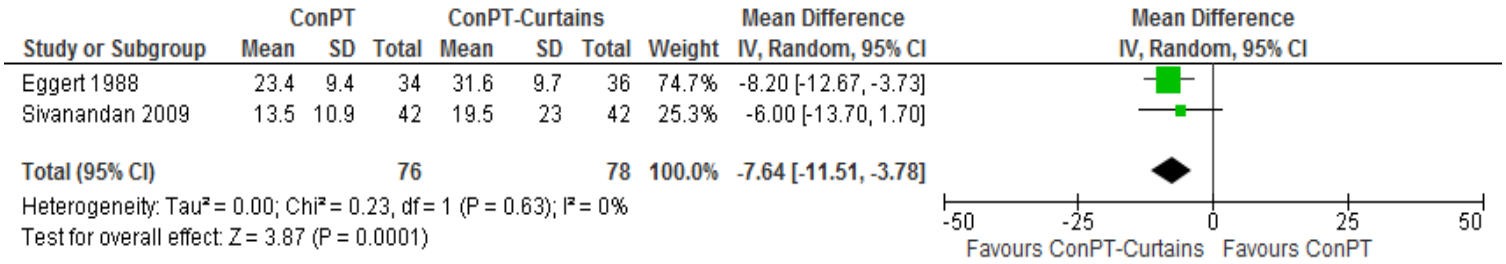
I.2.41 Conventional PT vs. Conventional PT + Curtains

2 Conventional PT vs. Conventional PT + Curtains: Mean duration of PT (hours) – Term only



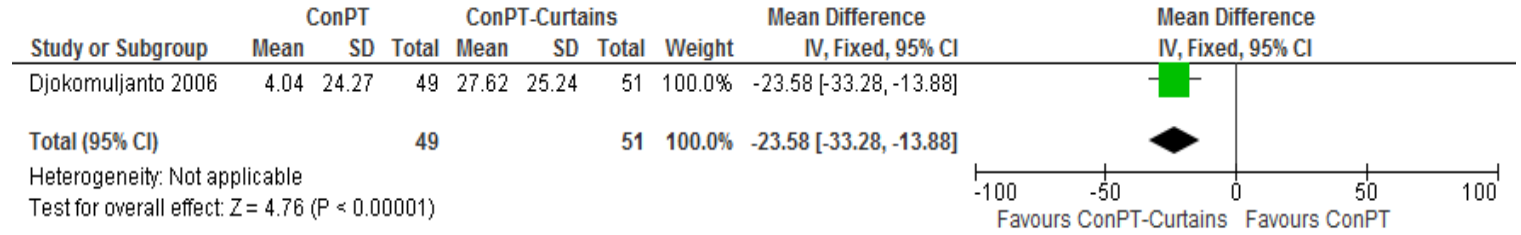
3

4 Conventional PT vs. Conventional PT + Curtains: Mean decrease in TSB from baseline after 24hrs PT (%) – Term only



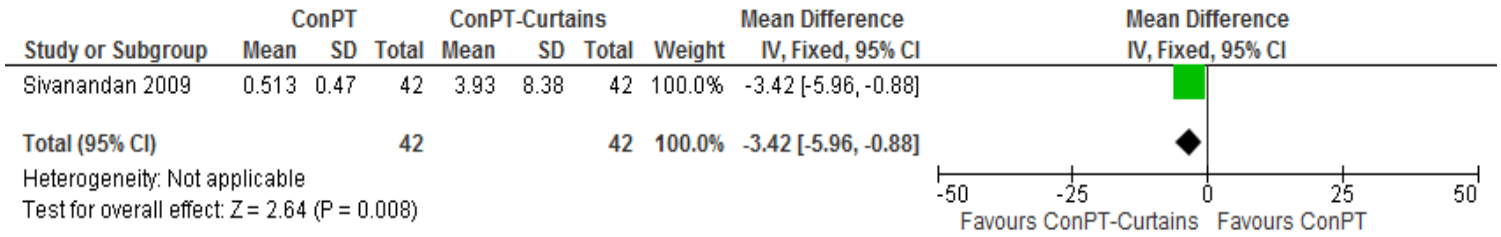
5

6 Conventional PT vs. Conventional PT + Curtains: Mean decrease in TSB from baseline after 4hrs PT (umol/L) – Term only



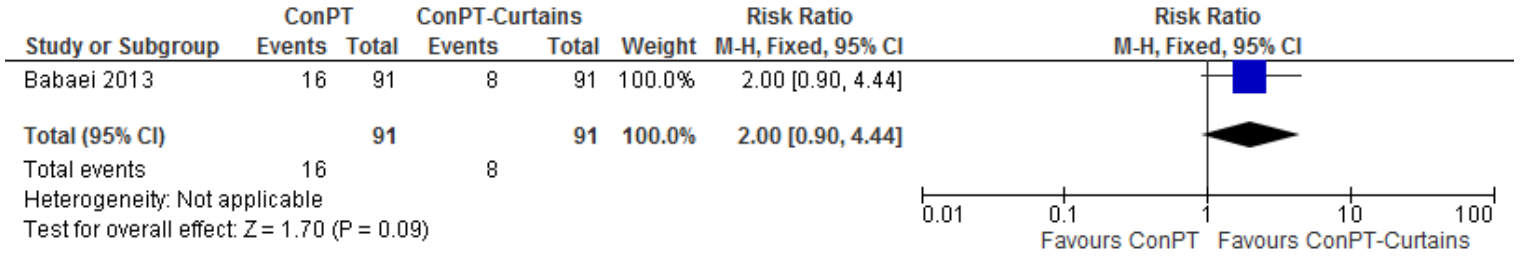
7

1 **Conventional PT vs. Conventional PT + Curtains: Mean decrease in TSB from baseline after 8hrs PT (umol/L) – Term only**



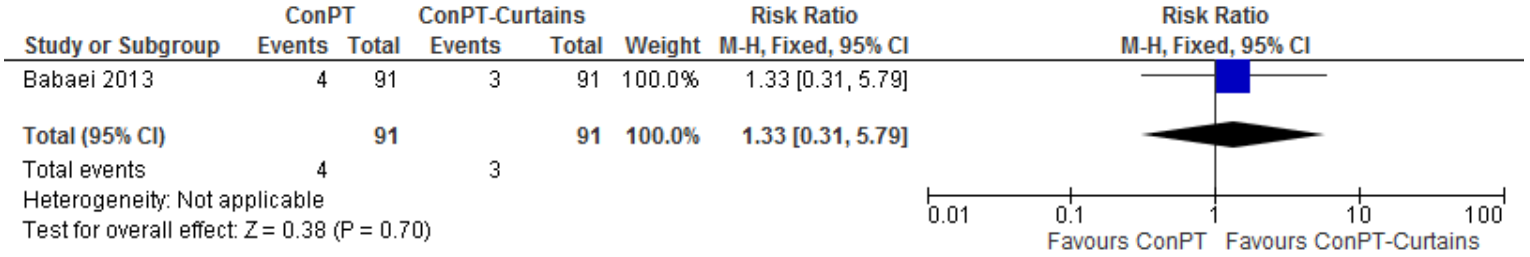
2

3 **Conventional PT vs. Conventional PT + Curtains: Skin rash – Term only**



4

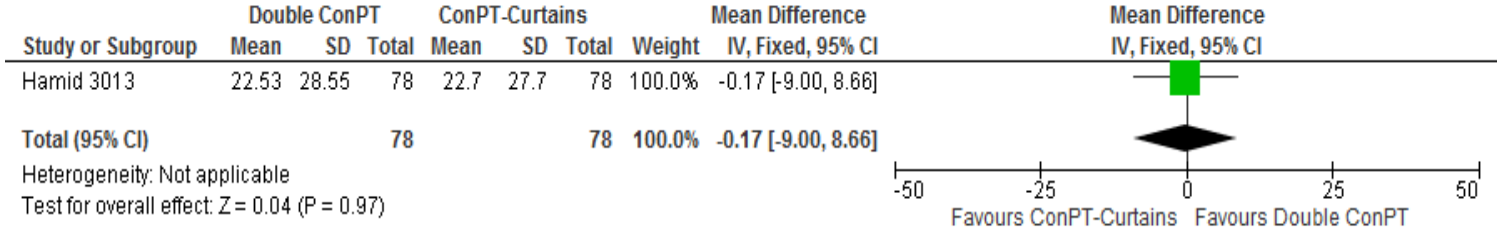
5 **Conventional PT vs. Conventional PT + Curtains: Hyperthemia – Term only**



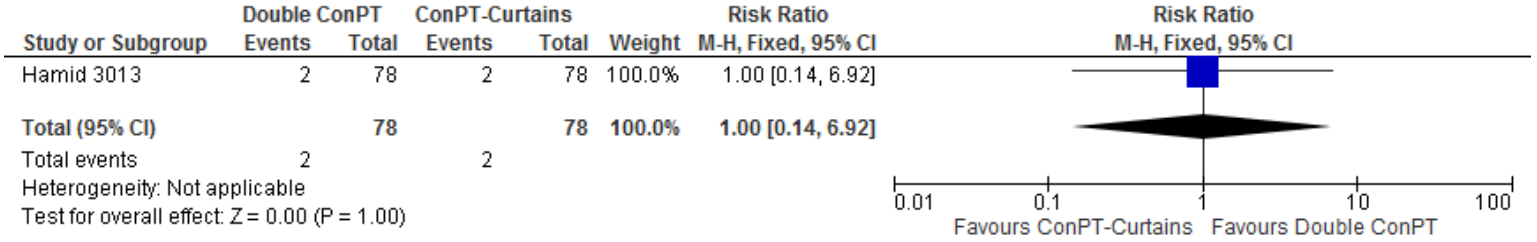
6

I.2.5 Double Conventional PT vs. Conventional PT + Curtains

Double Conventional PT vs. Conventional PT + Curtains: Mean decrease in TSB from baseline after 4hrs PT (umol/L) – Term only

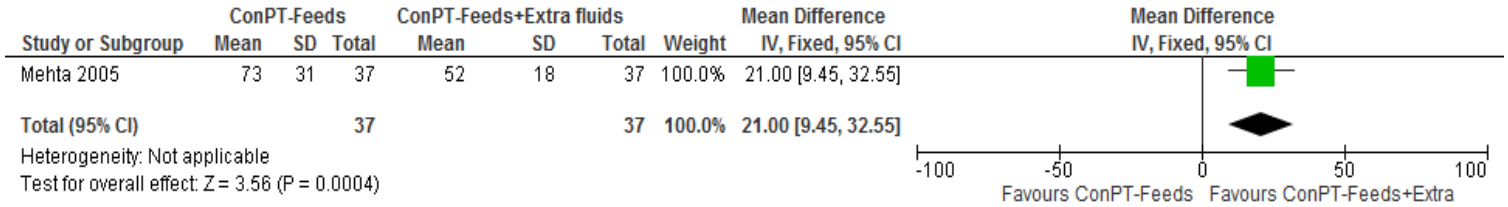


Double Conventional PT vs. Conventional PT + Curtains: Rebound jaundice – Term only

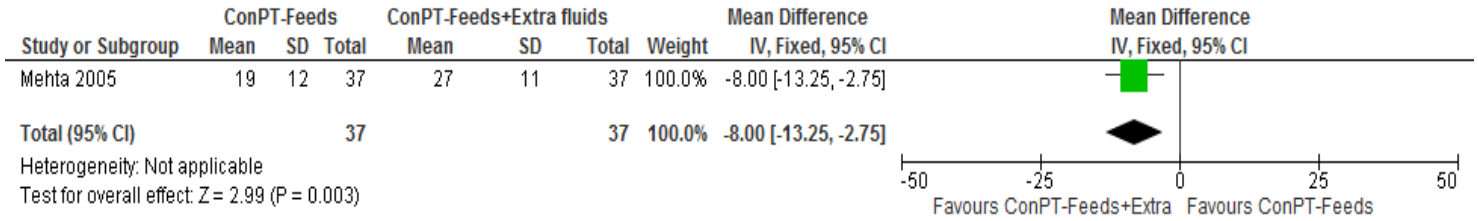


I.2.6 Conventional PT + Feeds vs. Conventional PT + Feeds + Extra fluids

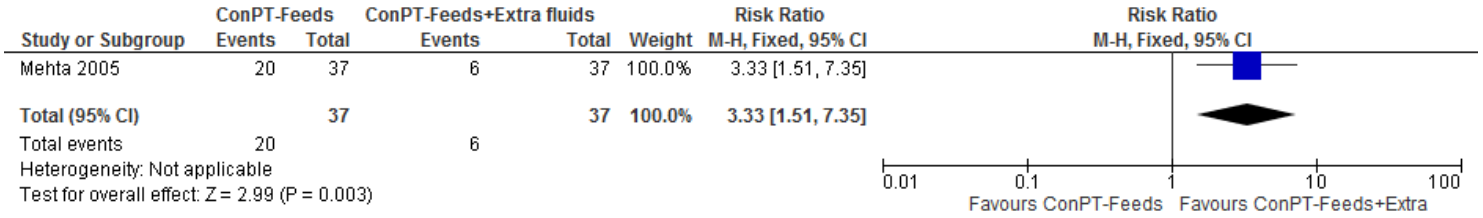
Conventional PT + Feeds vs. Conventional PT + Feeds + Extra fluids: Mean duration of PT (hours) – Term only



Conventional PT + Feeds vs. Conventional PT + Feeds + Extra fluids: Mean decrease in TSB from baseline after 24hrs PT (%) – Term only

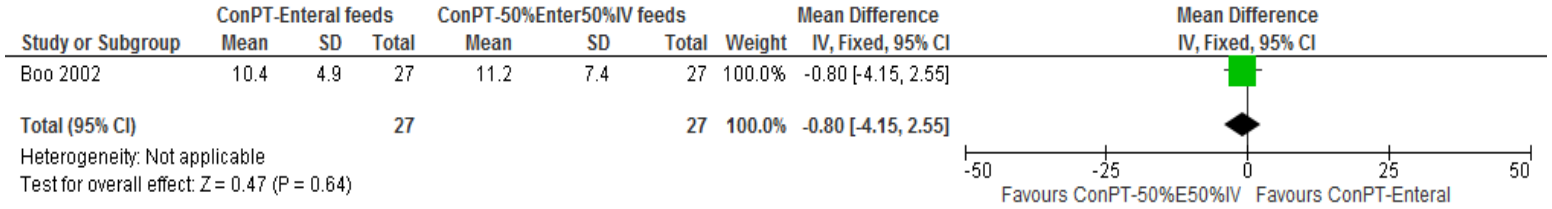


Conventional PT + Feeds vs. Conventional PT + Feeds + Extra fluids: Exchange transfusion – Term only

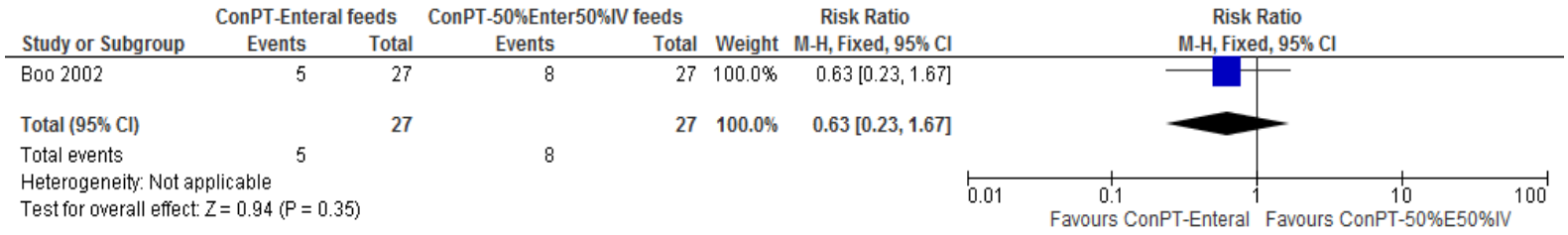


I.2.7 Conventional PT + Enteral feeds vs. Conventional PT + 50% Enteral & 50% IV feeds

Conventional PT + Enteral feeds vs. Conventional PT + 50% Enteral & 50% IV feeds: Mean decrease in iSB per hour of PT (umol/L/hour) – Term only

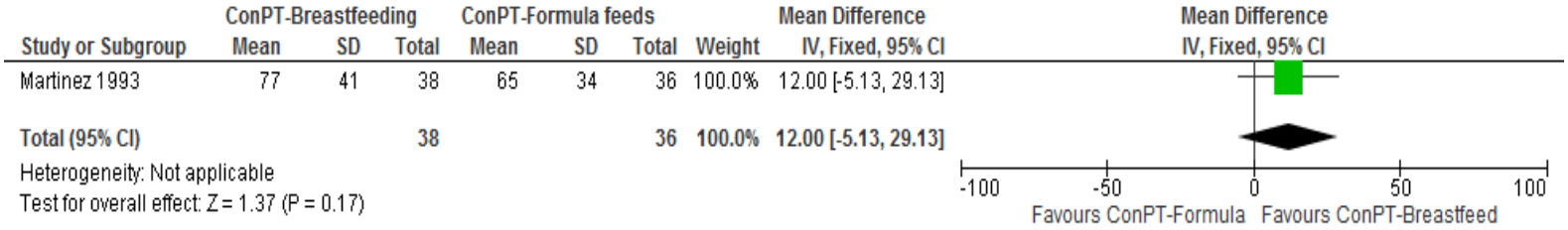


Conventional PT + Enteral feeds vs. Conventional PT + 50% Enteral & 50% IV feeds: Exchange transfusion – Term only



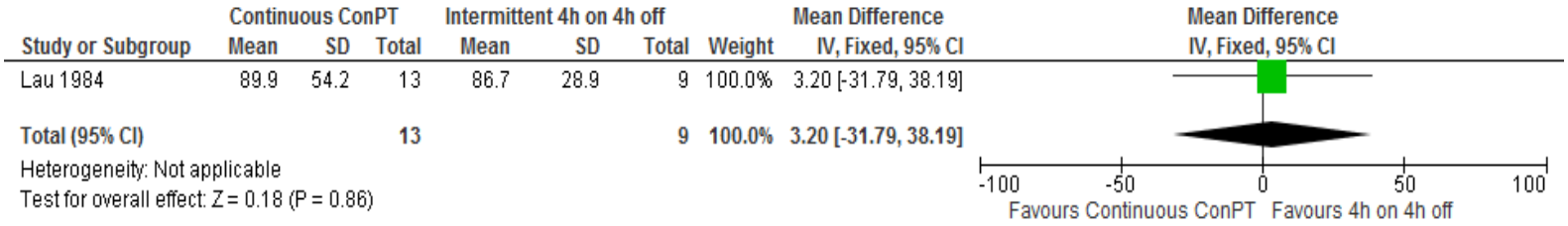
I.2.8 Conventional PT – Breastfeeding vs. Conventional PT – Formula feeds

Conventional PT – Breastfeeding vs. Conventional PT – Formula feeds: Mean decrease in TSB from baseline after 24hrs PT (umol/L) – Term only

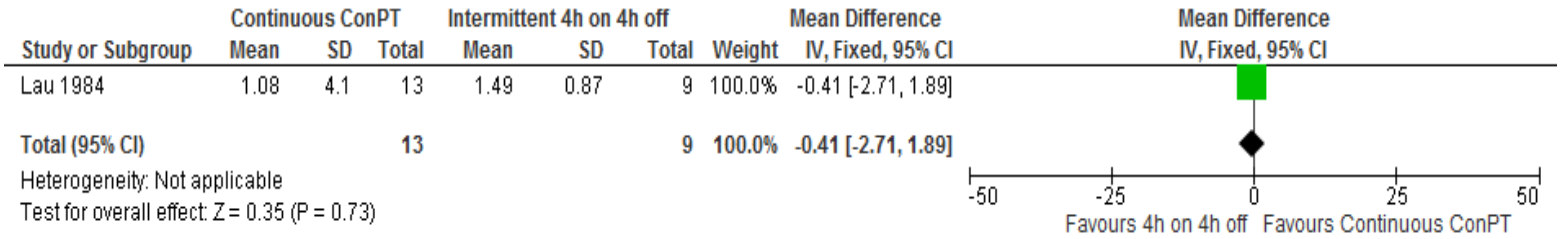


I.2.9 Continuous Conventional PT vs Intermittent Conventional PT (4 hrs on, 4 hrs off)

Continuous Conventional PT vs Intermittent Conventional PT (4 hrs on, 4 hrs off): Mean duration of PT (hour) – Term only

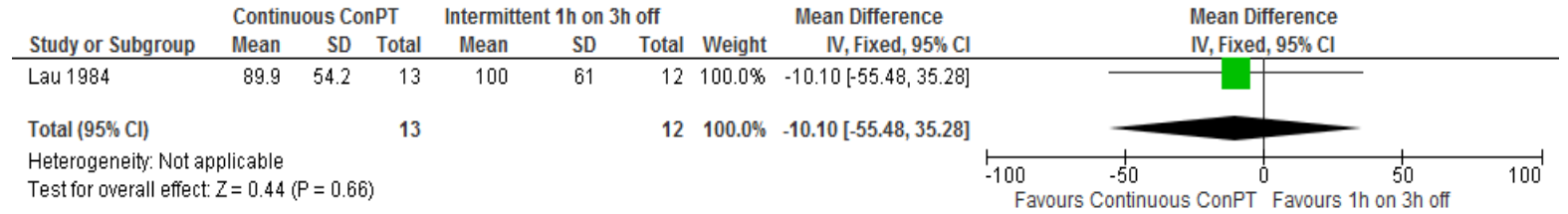


Continuous Conventional PT vs Intermittent Conventional PT (4 hrs on, 4 hrs off): Mean decrease in TSB per hour of PT (umol/L/hour) – Term only

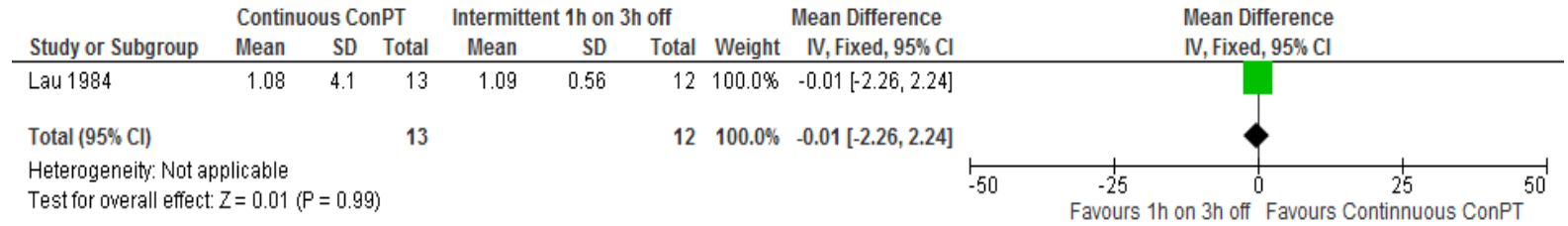


I.2.10 Continuous Conventional PT vs Intermittent Conventional PT (1 hr on, 3 hrs off)

Continuous Conventional PT vs Intermittent Conventional PT (1 hr on, 3 hrs off): Mean duration of PT (hour) – Term only

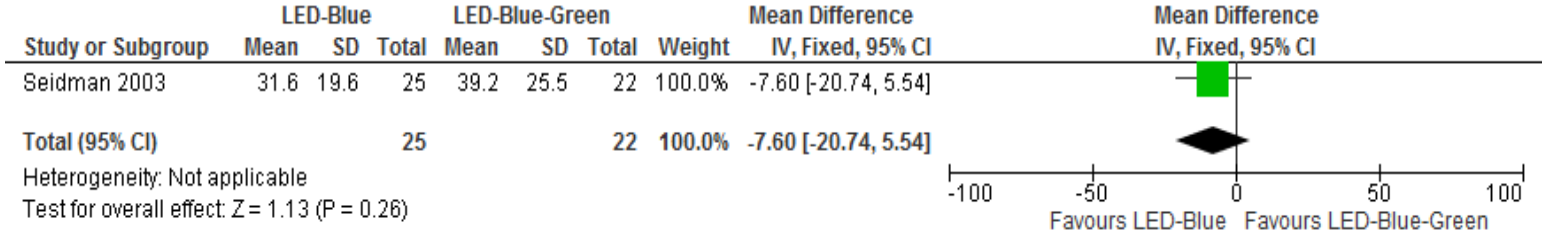


Continuous Conventional PT vs Intermittent Conventional PT (1 hr on, 3 hrs off): Mean decrease in TSB per hour of PT (umol/L/hour) – Term only

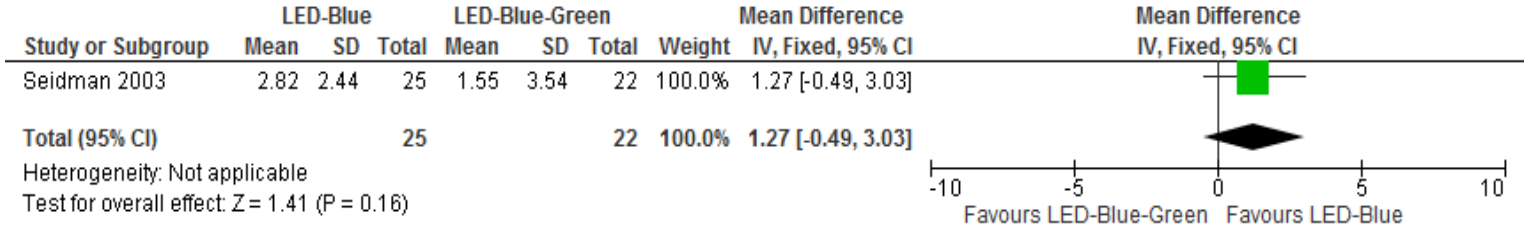


I.2.11 LED PT – Blue vs. LED PT – Blue-Green

LED PT – Blue vs. LED PT – Blue-Green: Mean duration of PT (hours) – Term only

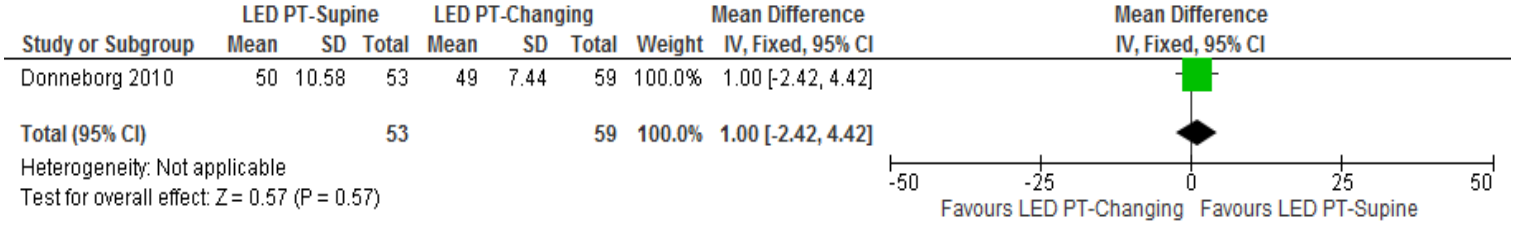


LED PT – Blue vs. LED PT – Blue-Green: Mean decrease in TSB per hour (umol/L/hour) – Term only



I.2.12 LED PT – Supine vs. LED PT – Changing

LED PT – Supine vs. LED PT – Changing: Mean decrease in TSB from baseline after 24hrs PT (%) – Term only



Appendix J: Economic search strategy

J.1 Review question 1 and 2

Databases that were searched, together with the number of articles retrieved from each database are shown in Table 22. The search strategy is shown in Table 23. The same strategy was translated for the other databases listed.

Table 22: Economic search summary, review question 1 and 2

Databases	Version/files	No. retrieved
NHS Economic Evaluation Database - NHS EED (Wiley)	Issue 1 of 4, January 2015	1
HTA (Wiley)	Issue 1 of 4, January 2015	4
MEDLINE (Ovid)	1946 to March Week 2 2015	70
MEDLINE In-Process (Ovid)	17 March 2015	9
EMBASE (Ovid)	1980 to 2015 Week 11	152

Table 23: Economic search strategy, review question 1 and 2

Line number/Search term/Number retrieved
1 exp Infant, Newborn/ (504810)
2 (newborn* or neonat* or preterm* or premature*).tw. (383416)
3 1 or 2 (701062)
4 Hyperbilirubinemia/ (3920)
5 exp Jaundice/ (11938)
6 Kernicterus/ (1043)
7 (bilirubin* or hyperbilirubin* or jaundice* or kernicterus* or icterus*).tw. (54370)
8 (bilirubin adj2 encephalopath*).tw. (355)
9 or/4-8 (60037)
10 Jaundice, Neonatal/ (5346)
11 Hyperbilirubinemia, Neonatal/ (571)
12 10 or 11 (5840)
13 3 and 9 (11190)
14 12 or 13 (12591)
15 exp Phototherapy/ (28850)
16 (phototherap* or heliotherap* or sunlight or actinotherap*).tw. (13507)
17 Fiber Optic Technology/ (13284)
18 (photoradiati* adj4 therap*).tw. (181)
19 ((light or fibre or ultraviolet) adj4 (therap* or technolog*)).tw. (4026)
20 (biliblanket* or bilibed* or bilisoft*).tw. (19)
21 (bilirubin adj4 (blanket* or pad*)).tw. (1)
22 (wallaby or wallabies).tw. (1137)
23 (optic adj2 fibre*).tw. (1321)
24 (light adj1 emitting adj1 diode*).tw. (2934)
25 (LED adj4 light*).tw. (1850)
26 ((fluorescen* or halogen*) adj4 (light* or lamp*)).tw. (7467)
27 (vickers adj4 flourescent*).tw. (0)
28 "mediprema cradle*".tw. (0)
29 neoblue*.tw. (3)
30 ((micro-lite or micro lite) adj4 phototherapy*).tw. (0)
31 ohmeda*.tw. (422)
32 medela*.tw. (19)
33 medestime*.tw. (0)
34 draeger*.tw. (178)

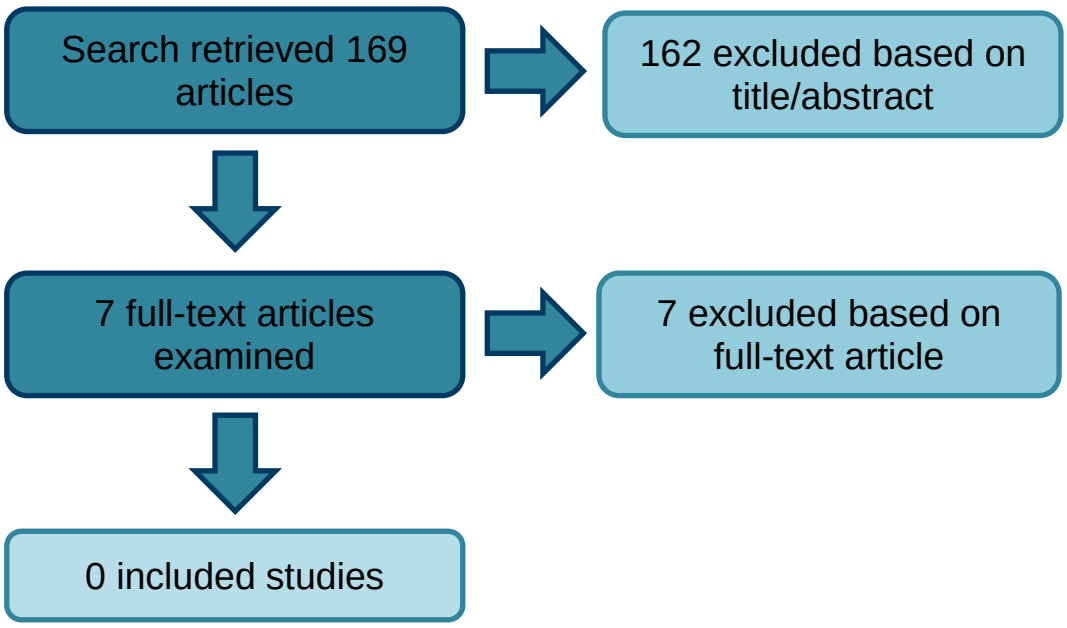
Line number/Search term/Number retrieved
35 (hill-rom* or hill rom*).tw. (35)
36 or/15-35 (65820)
37 14 and 36 (2037)
38 animals/ not human/ (3929323)
39 37 not 38 (2015)
40 limit 39 to english language (1615)
41 Economics/ (26593)
42 exp "Costs and Cost Analysis"/ (186660)
43 Economics, Dental/ (1858)
44 exp Economics, Hospital/ (20177)
45 exp Economics, Medical/ (13515)
46 Economics, Nursing/ (3913)
47 Economics, Pharmaceutical/ (2564)
48 Budgets/ (9930)
49 exp Models, Economic/ (10616)
50 Markov Chains/ (10303)
51 Monte Carlo Method/ (20799)
52 Decision Trees/ (9044)
53 econom$.tw. (161394)
54 cba.tw. (8829)
55 cea.tw. (16611)
56 cua.tw. (804)
57 markov$.tw. (12047)
58 (monte adj carlo).tw. (21500)
59 (decision adj3 (tree$ or analys$)).tw. (8624)
60 (cost or costs or costing$ or costly or costed).tw. (316511)
61 (price$ or pricing$).tw. (23714)
62 budget$.tw. (17706)
63 expenditure$.tw. (35926)
64 (value adj3 (money or monetary)).tw. (1376)
65 (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (2887)
66 or/41-65 (671973)
67 "Quality of Life"/ (124273)
68 quality of life.tw. (144078)
69 "Value of Life"/ (5433)
70 Quality-Adjusted Life Years/ (7450)
71 quality adjusted life.tw. (6269)
72 (qaly$ or qald$ or qale$ or qtime$).tw. (5162)
73 disability adjusted life.tw. (1252)
74 daly$.tw. (1228)
75 Health Status Indicators/ (20368)
76 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. (15829)
77 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (1010)
78 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (2765)
79 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (21)
80 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (336)
81 (euroqol or euro qol or eq5d or eq 5d).tw. (4130)
82 (qol or hql or hqol or hrqol).tw. (25822)
83 (hye or hyes).tw. (53)
84 health$ year$ equivalent$.tw. (38)
85 utilit$.tw. (115636)
86 (hui or hui1 or hui2 or hui3).tw. (877)
87 disutili$.tw. (222)

Line number/Search term/Number retrieved	
88	rosser.tw. (71)
89	quality of wellbeing.tw. (5)
90	quality of well-being.tw. (334)
91	qwb.tw. (173)
92	willingness to pay.tw. (2323)
93	standard gamble$.tw. (659)
94	time trade off.tw. (758)
95	time tradeoff.tw. (205)
96	tto.tw. (607)
97	or/67-96 (330155)
98	66 or 97 (957233)
99	40 and 98 (70)

1

Appendix K: Economic review flowchart

K.1 Review question 1 and 2



Appendix L:Economic excluded studies

L.1 Review question 1 and 2

Reference	Reason for exclusion
French S (2003) Phototherapy in the home for jaundiced neonates (Structured abstract). Health Technology Assessment Database : 15.	Could not obtain. Note this is an abstract reference identified by the search.
HAYES, Inc (2007) Phototherapy blankets versus standard phototherapy lights for the treatment of neonatal hyperbilirubinemia (Structured abstract). Health Technology Assessment Database	Could not obtain. Note this is an abstract reference identified by the search.
Ip S, Glicken S, Kulig J et al. (2002) Management of neonatal hyperbilirubinemia (Structured abstract). Health Technology Assessment Database	Systematic review only. No included economic studies. No original modelling.
Jackson CL, Tudehope D, Willis L et al. (2000) Home phototherapy for neonatal jaundice--technology and teamwork meeting consumer and service need. Australian Health Review 23: 162-8.	Not applicable
Malwade US, Jardine LA (2014) Home- versus hospital-based phototherapy for the treatment of non-haemolytic jaundice in infants at more than 37 weeks' gestation. [Review]. Cochrane Database of Systematic Reviews 6: CD010212.	Systematic review. No included economic studies.
TNO (1999) Home care of baby jaundice with phototherapy: intermediary report (Structured abstract). Health Technology Assessment Database	Could not obtain. Note this is an abstract reference identified by the search.
Viau CJ, Rountree C, Destarac MA et al. (2012) Prospective randomized controlled study comparing low-cost LED and conventional phototherapy for treatment of neonatal hyperbilirubinemia. Journal of Tropical Pediatrics 58: 178-83.	No economic analysis