Jaundice in newborn babies under 28 days

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NICE guideline: short version Draft for consultation, January 2016

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This guideline covers the care of newborn babies (from birth to 28 days) with jaundice.

Who is it for?

- Newborn babies with jaundice, and their parents and carers.
- Healthcare professionals working in primary, secondary and tertiary care.
- Commissioners and providers of neonatal jaundice services.

This guideline will update NICE guideline CG98 (published May 2010).

We have updated and added new recommendations on diagnosing and treating jaundice in newborn babies.

You are invited to comment on the new and updated recommendations on diagnosis in this guideline. These are **not shaded in grey** and are marked as:

- [new 2016] if the evidence has been reviewed and the recommendation has been added or updated or
- [2016] 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.

New recommendations on treatment were available for consultation in August

2015. These recommendations are shaded in grey and marked as **[new 2016]**. We cannot accept comments on these recommendations.

We have not updated recommendations shaded in grey and marked as **[2010]**, and cannot accept comments on them. In some cases, we have made minor wording changes for clarification.

See Update information for a full explanation of what is being updated.

This version of the guideline contains the draft recommendations, context and recommendations for research.

Information about how the recommendations on diagnosis were developed is on the <u>guideline's page for diagnosis</u> on the NICE website. This includes the guideline committee's discussion and the evidence reviews, the scope, and details of the committee and any declarations of interest.

Information about how the recommendations on treatment were developed is on the <u>quideline's page for treatment</u> on the NICE website.

Evidence for the 2010 recommendations is in the <u>full version</u> of the 2010 guideline. The supporting information and evidence for the 2016 recommendations are contained in an addendum covering diagnosis and treatment.

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1 Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in <u>Your care</u>.

<u>Using NICE guidelines to make decisions</u> explains how we use words to show the strength of our recommendations, and has information about safeguarding, consent and prescribing medicines (including 'off-label' use).

2 Threshold table

3 Consensus-based bilirubin thresholds for management of babies

4 38 weeks or more gestational age with hyperbilirubinaemia

Age (hours)	Bilirubin measurement (m	nicromol/litre)
0	> 100	> 100
6	> 125	> 150
12	> 150	> 200
18	> 175	> 250
24	> 200	> 300
30	> 212	> 350
36	> 225	> 400
42	> 237	> 450
48	> 250	> 450
54	> 262	> 450
60	> 275	> 450
66	> 287	> 450
72	> 300	> 450
78	> 312	> 450
84	> 325	> 450
90	> 337	> 450
96+	> 350	> 450
Action	Start phototherapy	Perform an exchange
		transfusion unless the
		bilirubin level falls below
		threshold while the
		treatment is being
		prepared

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2	1.1.1	Offer parents or carers information about neonatal jaundice that is
3		tailored to their needs and expressed concerns. This information
4		should be provided through verbal discussion backed up by written
5		information. Care should be taken to avoid causing unnecessary
6		anxiety to parents or carers. Information should include:
7		 factors that influence the development of significant
8		hyperbilirubinaemia
9		 how to check the baby for jaundice
10		what to do if they suspect jaundice
11		• the importance of recognising jaundice in the first 24 hours and
12		of seeking urgent medical advice
13		the importance of checking the baby's nappies for dark urine or
14		pale chalky stools
15		• the fact that neonatal jaundice is common, and reassurance that
16		it is usually transient and harmless
17		reassurance that breastfeeding can usually continue. [2010]
18	1.2	Care for all babies
10	1.2	Care for all bables
19	1.2.1	Identify babies as being more likely to develop significant
20		hyperbilirubinaemia if they have any of the following factors:
21		gestational age under 38 weeks
22		a previous sibling with neonatal jaundice requiring phototherapy
23		mother's intention to breastfeed exclusively
24		 visible jaundice in the first 24 hours of life. [2010]

Information for parents or carers

1	1.2.2	Ensure that adequate support is offered to all women who intend to
2		breastfeed exclusively. See the NICE guideline on postnatal care
3		for information on breastfeeding support. [2010]
4	1.2.3	In all babies:
5		check whether there are factors associated with an increased
6 7		likelihood of developing significant hyperbilirubinaemia soon after birth
8		 examine the baby for jaundice at every opportunity especially in
9		the first 72 hours. [2010]
10	1.2.4	Parents, carers and healthcare professionals should all look for
11		jaundice (visual inspection) in babies. [2016]
12	1.2.5	When looking for jaundice (visual inspection):
13		 check the naked baby in bright and preferably natural light
14		• examine the sclerae and gums, and press lightly on the skin to
15		check for signs of jaundice in 'blanched' skin. [2016]
16	1.2.6	Do not rely on visual inspection alone to estimate the bilirubin level
17		in a baby with suspected jaundice. [2016]
18	1.2.7	Do not measure bilirubin levels routinely in babies who are not
19		visibly jaundiced. [2010]
20	1.2.8	Do not use any of the following to predict significant
21		hyperbilirubinaemia:
22		umbilical cord blood bilirubin level
23		end-tidal carbon monoxide (ETCOc) measurement
24		 umbilical cord blood direct antiglobulin test (DAT) (Coombs'
25		test). [2010]

1 Additional care

2 3 4 5	1.2.9	Ensure babies with factors associated with an increased likelihood of developing significant hyperbilirubinaemia receive an additional visual inspection by a healthcare professional during the first 48 hours of life. [2010]
6 7	Urgent ac	dditional care for babies with visible jaundice in the first
8 9 10	1.2.10	In all babies with suspected or obvious jaundice in the first 24 hours of life, measure and record the serum bilirubin level urgently (within 2 hours). [2010]
11 12 13	1.2.11	In all babies with suspected or obvious jaundice in the first 24 hours of life, continue to measure the serum bilirubin level every 6 hours until the level is both:
14 15		 below the treatment threshold stable and/or falling. [2010]
16 17 18 19	1.2.12	Arrange a referral to ensure that an urgent medical review is conducted (as soon as possible and within 6 hours) for babies with suspected or obvious jaundice in the first 24 hours of life to exclude pathological causes of jaundice. [2010]
20 21 22	1.2.13	Interpret bilirubin levels according to the baby's postnatal age in hours and manage hyperbilirubinaemia according to the threshold and the treatment threshold graphs . [2010]

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Care for babies more than 24 hours old

2	1.2.14	Measure and record the bilirubin level urgently (within 6 hours) in
3		all babies more than 24 hours old with suspected or obvious
4		jaundice. [2010]
5	How to n	neasure the bilirubin level
6	1.2.15	Use serum bilirubin measurement for babies:
7		• in the first 24 hours of life or
8		 who have a gestational age of less than 35 weeks. [2016]
9	1.2.16	In babies who have a gestational age of 35 weeks or more and who
10		are over 24 hours old:
11		use a transcutatneous bilirubinometer to measure the bilirubin
12		level
13		• if a transcutaneous bilirubinometer is not available, measure the
14		serum bilirubin
15		 if a transcutaneous bilirubinometer measurement indicates a
16		bilirubin level greater than 250 micromol/litre, measure the
17		serum bilirubin to check the result
18		 use serum bilirubin measurement if bilirubin levels are at or
19		above the relevant treatment thresholds for their age, and for all
20		subsequent measurements. [2016]
21	1.2.17	Do not use an icterometer to measuer bilirubin levels in babies.
22		[2016]

1	1.3	Management and treatment of hyperbilirubinaemia
2	Informati	on for parents or carers on treatment
3	1.3.1	Offer parents or carers information about treatment for hyperbilirubinaemia, including:
5 6 7		 anticipated duration of treatment reassurance that breastfeeding, nappy-changing and cuddles can usually continue. [2010]
8 9	1.3.2	Encourage mothers of breastfed babies with jaundice to breastfeed frequently, and to wake the baby for feeds if necessary. [2010]
10 11	1.3.3	Provide lactation/feeding support to breastfeeding mothers whose baby is visibly jaundiced. [2010]
12	How to m	anage hyperbilirubinaemia
13 14 15	1.3.4	Use the bilirubin level to determine the management of hyperbilirubinaemia in all babies (see the <u>threshold table</u> and the <u>treatment threshold graphs</u>). [2010]
16 17	1.3.5	Do not use the albumin/bilirubin ratio when making decisions about the management of hyperbilirubinaemia. [2010]
18 19 20 21	1.3.6	Do not subtract conjugated bilirubin from total serum bilirubin when making decisions about the management of hyperbilirubinaemia (see management thresholds in the threshold table and the treatment threshold graphs). [2010]
22 23	1.4	Measuring and monitoring bilirubin thresholds before and during phototherapy
24	Before st	arting phototherapy

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1.4.1

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In babies who are clinically well, have a gestational age of

38 weeks or more and are more than 24 hours old, and who have a

1		serum bilirubin level that is below the phototherapy threshold but
2		within 50 micromol/litre of the threshold (see the threshold table
3		and the treatment threshold graphs), repeat serum bilirubin
4		measurement as follows:
5		within 18 hours for babies with risk factors for neonatal jaundice
6		(those with a sibling who had neonatal jaundice that needed
7		phototherapy or a mother who intends to exclusively breastfeed)
8		• within 24 hours for babies without risk factors. [new 2016]
9	1.4.2	In babies who are clinically well, have a gestational age of
10		38 weeks or more and are more than 24 hours old, and who have a
11		serum bilirubin level that is below the phototherapy threshold by
12		more than 50 micromol/litre (see the threshold table and the
13		treatment threshold graphs), do not repeat serum bilirubin
14		measurement. [new 2016]
15	1.4.3	Do not use phototherapy in babies whose bilirubin does not exceed
16		the phototherapy threshold levels in the threshold table and the
17		treatment threshold graphs. [2010]
18	During p	hototherapy
19	1.4.4	During phototherapy:
30		
20		 repeat serum bilirubin measurement 4–6 hours after initiating
21		phototherapy
22		 repeat serum bilirubin measurement every 6–12 hours when the
23		serum bilirubin level is stable or falling. [2010]

Stopping phototherapy

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2	1.4.5	Stop phototherapy once serum bilirubin has fallen to a level at least
3		50 micromol/litre below the phototherapy threshold (see threshold
4		table and the treatment threshold graphs). [2010]
5	1.4.6	Check for rebound of significant hyperbilirubinaemia with a repeat
6		serum bilirubin measurement 12–18 hours after stopping
7		phototherapy. Babies do not necessarily have to remain in hospital
8		for this to be done. [2010]

Type of phototherapy to use

10	1.4.7	Do not use sunlight as treatment for hyperbilirubinaemia. [2010]
11	1.4.8	Use phototherapy ¹ to treat significant hyperbilirubinaemia (see the
12		threshold table and the treatment threshold graphs) in babies. [new
13		2016]
14	1.4.9	Consider intensified phototherapy ² to treat significant
15		hyperbilirubinaemia in babies if any of the following apply [new
16		2016]:
17		 the serum bilirubin level is rising rapidly (more than
18		
10		8.5 micromol/litre per hour)
19		 8.5 micromol/litre per hour) the serum bilirubin is at a level within 50 micromol/litre below the
19		the serum bilirubin is at a level within 50 micromol/litre below the
19 20		the serum bilirubin is at a level within 50 micromol/litre below the threshold for which exchange transfusion is indicated after
19 20 21		 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 the treatment threshold
19 20 21 22		 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 the treatment threshold graphs)

¹ Phototherapy given using an artificial light source with an appropriate spectrum and irradiance. This can be delivered using light-emitting diode (LED), fibreoptic or fluorescent lamps, tubes or bulbs.

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² 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 2 3	1.4.10	If the serum bilirubin level falls during intensified phototherapy to a level 50 micromol/litre below the threshold for which exchange
3	Informati	transfusion is indicated reduce the intensity of phototherapy. [2010] on for parents or carers on phototherapy
7	morman	on for parents of carers on phototherapy
5 6	1.4.11	Offer parents or carers verbal and written information on phototherapy including all of the following:
7 8 9 10 11 12 13 14 15 16 17		 why phototherapy is being considered why phototherapy may be needed to treat significant hyperbilirubinaemia the possible adverse effects of phototherapy the need for eye protection and routine eye care reassurance that short breaks for feeding, nappy changing and cuddles will be encouraged what might happen if phototherapy fails rebound jaundice potential long-term adverse effects of phototherapy potential impact on breastfeeding and how to minimise this. [2010]
19	General o	care of the baby during phototherapy
20	1.4.12	During phototherapy:
21 22 23 24 25 26 27		 place the baby in a supine position unless other clinical conditions prevent this ensure treatment is applied to the maximum area of skin monitor the baby's temperature and ensure the baby is kept in an environment that will minimise energy expenditure (thermoneutral environment) monitor hydration by daily weighing of the baby and assessing
28		wet nappies

1 2		 support parents and carers and encourage them to interact with the baby. [2010]
3	1.4.13	Give the baby eye protection and routine eye care during phototherapy. [2010]
5 6 7	1.4.14	Use tinted headboxes as an alternative to eye protection in babies with a gestational age of 37 weeks or more undergoing phototherapy. [2010]
8	Monitorir	ng the baby during phototherapy
9	1.4.15	During phototherapy:
10 11 12 13 14 15		 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. [2016]
16	1.4.16	During intensified phototherapy:
17 18 19 20		 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.
21 22		Maternal expressed milk is the additional feed of choice if available, and when additional feeds are indicated. [2016]

Phototherapy equipment

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2		
_	1.4.17	Ensure all phototherapy equipment is maintained and used
3		according to the manufacturers' guidelines. [2010]
4	1.4.18	Use incubators or bassinets according to clinical need and
5		availability. [2010]
6	1.4.19	Do not use white curtains routinely with phototherapy as they may
7		impair observation of the baby. [2010]
8	1.5	Factors that influence the risk of kernicterus
9	1.5.1	Identify babies with hyperbilirubinaemia as being at increased risk
10		of developing kernicterus if they have any of the following:
11		a serum bilirubin level greater than 340 micromol/litre in babies
12		with a gestational age of 37 weeks or more
13		a rapidly rising bilirubin level of greater than 8.5 micromol/litre
14		per hour
15		 clinical features of acute bilirubin encephalopathy. [2010]
16	1.6	Formal assessment for underlying disease
16 17	1.6 1.6.1	Formal assessment for underlying disease In addition to a full clinical examination by a suitably trained
17		In addition to a full clinical examination by a suitably trained
17 18		In addition to a full clinical examination by a suitably trained healthcare professional, carry out all of the following tests in babies
17 18 19		In addition to a full clinical examination by a suitably trained healthcare professional, carry out all of the following tests in babies with significant hyperbilirubinaemia as part of an assessment for
17 18 19 20		In addition to a full clinical examination by a suitably trained healthcare professional, carry out all of the following tests in babies with significant hyperbilirubinaemia as part of an assessment for underlying disease (see threshold and the treatment threshold
17 18 19 20 21		In addition to a full clinical examination by a suitably trained healthcare professional, carry out all of the following tests in babies with significant hyperbilirubinaemia as part of an assessment for underlying disease (see threshold table and the treatment threshold graphs):
17 18 19 20 21		In addition to a full clinical examination by a suitably trained healthcare professional, carry out all of the following tests in babies with significant hyperbilirubinaemia as part of an assessment for underlying disease (see threshold table and the treatment threshold graphs): • serum bilirubin (for baseline level to assess response to
17 18 19 20 21 22 23		In addition to a full clinical examination by a suitably trained healthcare professional, carry out all of the following tests in babies with significant hyperbilirubinaemia as part of an assessment for underlying disease (see threshold table and the treatment): • serum bilirubin (for baseline level to assess response to treatment)
17 18 19 20 21 22 23 24		In addition to a full clinical examination by a suitably trained healthcare professional, carry out all of the following tests in babies with significant hyperbilirubinaemia as part of an assessment for underlying disease (see threshold table and the treatment threshold graphs): • serum bilirubin (for baseline level to assess response to treatment) • blood packed cell volume
17 18 19 20 21 22 23 24 25		In addition to a full clinical examination by a suitably trained healthcare professional, carry out all of the following tests in babies with significant hyperbilirubinaemia as part of an assessment for underlying disease (see threshold table and the treatment threshold graphs): • serum bilirubin (for baseline level to assess response to treatment) • blood packed cell volume • blood group (mother and baby)

1 2	1.6.2	When assessing the baby for underlying disease, consider whether the following tests are clinically indicated:						
2		the following tests are clinically indicated.						
3		full blood count and examination of blood film						
4		 blood glucose-6-phosphate dehydrogenase levels, taking 						
5		account of ethnic origin						
6		• microbiological cultures of blood, urine and/or cerebrospinal fluid						
7		(if infection is suspected). [2010]						
8	1.7	Care of babies with prolonged jaundice						
9	1.7.1	In babies with a gestational age of 37 weeks or more with jaundice						
10		lasting more than 14 days, and in babies with a gestational age of						
11		less than 37 weeks and jaundice lasting more than 21 days:						
12		look for pale chalky stools and/or dark urine that stains the						
13		nappy						
14		measure the conjugated bilirubin						
15		carry out a full blood count						
16		 carry out a blood group determination (mother and baby) and 						
17		DAT (Coombs' test). Interpret the result taking account of the						
18		strength of reaction, and whether mother received prophylactic						
19		anti-D immunoglobulin during pregnancy						
20		 carry out a urine culture 						
21		 ensure that routine metabolic screening (including screening for 						
22		congenital hypothyroidism) has been performed. [2010]						
22		congenital hypothyroidism) has been penomied. [2010]						
23	1.7.2	Follow expert advice about care for babies with a conjugated						
24		bilirubin level greater than 25 micromol/litre because this may						
25		indicate serious liver disease. [2010]						
26	1.8	Intravenous immunoglobulin						
27	1.8.1	Use intravenous immunoglobulin (IVIG) (500 mg/kg over 4 hours)						
28		as an adjunct to continuous intensified phototherapy in cases of						
29		rhesus haemolytic disease or ABO haemolytic disease when the						

1 2		serum bilirubin continues to rise by more than 8.5 micromol/litre per hour. [2010]
3	1.8.2	Offer parents or carers information on IVIG including:
4 5 6 7 8		 why IVIG is being considered why IVIG may be needed to treat significant hyperbilirubinaemia the possible adverse effects of IVIG when it will be possible for parents or carers to see and hold the baby. [2010]
9	1.9	Exchange transfusion
10 11	1.9.1	Offer parents or carers information on exchange transfusion including:
12 13 14 15 16 17 18		 the fact that exchange transfusion requires that the baby be admitted to an intensive care bed why an exchange transfusion is being considered why an exchange transfusion may be needed to treat significant hyperbilirubinaemia the possible adverse effects of exchange transfusions when it will be possible for parents or carers to see and hold the baby after the exchange transfusion. [2010]
20	1.9.2	Use a double-volume exchange transfusion to treat babies:
21 22 23 24		 whose serum bilirubin level indicates its necessity (see threshold and the treatment threshold graphs) and/or with clinical features and signs of acute bilirubin encephalopathy. [2010]
25	1.9.3	During exchange transfusion do not:
26 27 28		 stop continuous intensified phototherapy perform a single-volume exchange use albumin priming

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1		routinely administer intravenous calcium. [2010]
2	1.9.4	Following evolungs transfusion:
2	1.9.4	Following exchange transfusion:
3		maintain continuous intensified phototherapy
4		measure serum bilirubin level within 2 hours and manage
5		according to the threshold table and the treatment threshold
6		<u>graphs</u> . [2010]
7	1.10	Other therapies
8	1.10.1	Do not use any of the following to treat hyperbilirubinaemia:
9		• agar
10		albumin
11		barbiturates
12		• charcoal
13		cholestyramine
14		• clofibrate
15		D-penicillamine
16		• glycerin
17		• manna
18		metalloporphyrins
19		• riboflavin
20		traditional Chinese medicine
21		acupuncture
22		• homeopathy. [2010]
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2.4		

Context

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^		•	. (()			conditions				•
,	IOLIDAIOO	10 ANA	OT TOO	mact	α	CONCITIONS	naaaina	$m \cap \alpha \cap \alpha \cap$	OTTO DTI OD	ın
/		15 UHE	()	111051				$\Pi \cup \Box \cup \Box \cup \Box \cup \Box$	anennon	

- 3 newborn babies. Jaundice refers to the yellow colouration of the skin and the
- 4 sclerae (whites of the eyes) caused by the accumulation of bilirubin in the skin
- 5 and mucous membranes. It is caused by a raised level of bilirubin in the body,
- 6 a condition known as hyperbilirubinaemia.
- 7 Approximately 60% of term and 80% of preterm babies develop jaundice in
- 8 the first week of life, and about 10% of breastfed babies are still jaundiced at
- 9 1 month. For most babies, jaundice is not an indication of an underlying
- disease, and this early jaundice (termed 'physiological jaundice') is usually
- 11 harmless.
- 12 Breastfed babies are more likely than bottle-fed babies to develop
- physiological jaundice within the first week of life. Prolonged jaundice that is,
- jaundice persisting beyond the first 14 days is also seen more commonly in
- breastfed babies. Prolonged jaundice is usually harmless, but can sometimes
- be an indication of serious liver disease.
- 17 Jaundice has many possible causes, including blood group incompatibility
- 18 (most commonly rhesus or ABO incompatibility), other causes of haemolysis
- 19 (breaking down of red blood cells), sepsis (infection), liver disease, bruising
- and metabolic disorders. Deficiency of a particular enzyme, glucose-6-
- 21 phosphate-dehydrogenase, can cause severe neonatal jaundice. Glucose-6-
- 22 phosphate-dehydrogenase deficiency is more common in certain ethnic
- 23 groups and runs in families.
- 24 Bilirubin is mainly produced from the breakdown of red blood cells. Red cell
- breakdown produces unconjugated (or 'indirect') bilirubin, which circulates
- 26 mostly bound to albumin although some is 'free' and hence able to enter the
- 27 brain. Unconjugated bilirubin is metabolised in the liver to produce conjugated
- 28 (or 'direct') bilirubin which then passes into the gut and is largely excreted in
- 29 stool. The terms direct and indirect refer to the way the laboratory tests
- 30 measure the different forms. Some tests measure total bilirubin and do not
- 31 distinguish between the two forms.

- 1 In young babies, unconjugated bilirubin can penetrate the membrane that lies
- 2 between the brain and the blood (the blood-brain barrier). Unconjugated
- 3 bilirubin is potentially toxic to neural tissue (brain and spinal cord). Entry of
- 4 unconjugated bilirubin into the brain can cause both short-term and long-term
- 5 neurological dysfunction (bilirubin encephalopathy). The term kernicterus is
- 6 used to denote the clinical features of acute or chronic bilirubin
- 7 encephalopathy, as well as the yellow staining in the brain associated with the
- 8 former. The risk of kernicterus is increased in babies with extremely high
- 9 bilirubin levels. Kernicterus is also known to occur at lower levels of bilirubin in
- term babies who have risk factors, and in preterm babies.
- 11 Clinical recognition and assessment of jaundice can be difficult, particularly in
- babies with darker skin tones. Once jaundice is recognised, there is
- uncertainty about when to treat, and there is widespread variation in the use
- of phototherapy and exchange transfusion. There is a need for more uniform,
- 15 evidence-based practice and for consensus-based practice where such
- 16 evidence is lacking. This guideline provides guidance regarding the
- 17 recognition, assessment and treatment of neonatal jaundice. The advice is
- based on evidence where this is available and on consensus-based practice
- where it is not.
- 20 The NICE guideline on jaundice in newborn babies under 28 days (NICE
- 21 guideline CG98) was reviewed in May 2014 as part of NICE's routine
- 22 surveillance programme to decide whether it needed updating. The
- 23 surveillance report identified new evidence relating to three areas of the
- 24 guidance:
- the best modality for giving phototherapy
- the correct procedure for administering phototherapy
- the accuracy of tests for recognising neonatal jaundice.
- 28 The topic experts recruited to join the Clinical Guidelines Update Committee
- 29 for this topic further expressed concern that the consensus-based bilirubin
- 30 thresholds specified in the original NICE guideline on neonatal jaundice were
- 31 not implemented by clinicians and midwives for the following reasons:

- some of the bilirubin thresholds relating to retesting and consideration for
- 2 phototherapy are too conservative
- repeat measurements of bilirubin before phototherapy (in 6-12 hours) as
- 4 recommended by the consensus-based thresholds table are too resource
- 5 intensive, particularly for community midwives
- the public consultation in 2010 did not manage to engage fully the
- stakeholders, clinicians and midwives who would use the thresholds table
- 8 on a day-to-day basis.
- 9 It was therefore decided to that the this section of the guideline also needed to
- 10 be updated.
- 11 The guideline will assume that prescribers will use a drug's summary of
- 12 product characteristics to inform decisions made with individual patients.

13 Recommendations for research

- 14 In 2010, the guideline committee made the following recommendations for
- 15 research.
- As part of the 2016 update, the standing committee made an additional
- 17 research recommendation on parent and staff experience of phototherapy.
- 18 This can be found in the addendum.

19 1 Breastfeeding and hyperbilirubinaemia

- 20 What are the factors that underlie the association between breastfeeding and
- 21 jaundice?

Why this is important

- 23 Breastfeeding has been shown to be a factor in significant
- 24 hyperbilirubinaemia. The reasons for this association have not yet been fully
- 25 elucidated.
- 26 This question should be answered by studying infants in the first 28 days of
- 27 life receiving different feeding types (breast milk, formula feeds or mixed
- 28 feeds). Infants who do not develop significant hyperbilirubinaemia should be

- 1 compared with infants with significant hyperbilirubinaemia. The outcomes
- 2 chosen should include maternal factors, neonatal factors and blood analyses.

2 Trancutaneous bilirubin screening and risk factors

- 4 What is the comparative effectiveness and cost-effectiveness of universal pre-
- 5 discharge transcutaneous bilirubin screening alone or combined with a risk
- 6 assessment in reducing jaundice-related neonatal morbidity and hospital
- 7 readmission?

8 Why this is important

- 9 There is good evidence that a risk assessment that combines the result of a
- timed transcutaneous bilirubin level with risk factors for significant
- 11 hyperbilirubinaemia is effective at preventing later significant
- 12 hyperbilirubinaemia.
- 13 This question should be answered by studying the effects of timed pre-
- 14 discharge transcutaneous bilirubin levels and timed pre-discharge
- transcutaneous bilirubin levels combined with risk assessment. The study
- population should consist of babies in the first 28 days of life, with subgroups
- including near-term babies and babies with dark skin tones. The interventions
- should be compared with standard care (discharge without timed
- 19 transcutaneous bilirubin level), and the outcomes chosen should include
- significant hyperbilirubinaemia, cost-effectiveness and parental anxiety.

21 3 Transcutaneous bilirubinometers

- What is the comparative accuracy of the Minolta JM-103 and the BiliChek
- when compared to serum bilirubin levels in all babies?

24 Why this is important

- 25 The accuracy of transcutaneous bilirubinometers (Minolta JM-103 and
- 26 BiliChek) has been adequately demonstrated in term babies below treatment
- 27 levels (bilirubin less than 250 micromol/litre). New research is needed to
- evaluate the accuracy of different transcutaneous bilirubinometers in
- comparison to serum bilirubin levels in all babies.

- 1 This question should be answered by comparing bilirubin levels taken using
- 2 different transcutaneous bilirubinometers with bilirubin levels assessed using
- 3 serum (blood) tests. The study population should comprise babies in the first
- 4 28 days of life, with subgroups including preterm babies, babies with dark skin
- 5 tones, babies with high levels of bilirubin and babies after phototherapy. The
- 6 outcomes chosen should include diagnostic accuracy (sensitivity, specificity,
- 7 positive predictive value, negative predictive value), parental anxiety, staff and
- 8 parental satisfaction with test and cost effectiveness.

9 4 Interruptions during phototherapy

- How frequently and for how long can phototherapy be interrupted without
- 11 adversely effecting clinical outcomes?

12 Why this is important

- 13 The effectiveness and tolerability of intermittent phototherapy has been
- 14 adequately demonstrated in term babies at low treatment levels (bilirubin less
- than 250 micromol/litre). New research is needed to evaluate the
- 16 effectiveness and tolerability of different frequencies of interruptions of
- 17 different durations.
- 18 The study population should comprise babies in the first 28 days of life in
- 19 phototherapy. Interruptions of 45 or 60 minutes would be made either on
- demand, every hour or every 2 hours, and compared with interruptions of up
- 21 to 30 minutes every 3 hours. The outcomes chosen should include
- 22 effectiveness in terms of the mean decrease in bilirubin levels and the mean
- 23 duration of phototherapy. Extra outcomes could include adverse effects,
- 24 parental bonding and parental anxiety, staff and parental satisfaction with
- 25 treatment and cost effectiveness.

26 5 National registries

- National registries are needed of cases of significant hyperbilirubinaemia,
- 28 kernicterus and exchange transfusions.

1 Why this is important

- 2 There is good evidence that prospective surveys in the UK and data from a
- 3 national kernicterus register in the US can help to identify root causes of
- 4 kernicterus and acute bilirubin encephalopathy.
- 5 The study population should comprise all children with a peak bilirubin level
- 6 greater than 450 micromol/litre, which is the threshold for an exchange
- 7 transfusion recommended by NICE. The intervention would be maternal,
- 8 prenatal, perinatal and neonatal factors. The outcomes chosen should be
- 9 shortcomings in clinical and service provision to prevent recurring themes in
- 10 kernicterus cases.

11 6 Parent and healthcare professional experience of

12 **phototherapy**

- What is the experience and acceptability of phototherapy from the
- persepective of parents and healthcare professionals?

15 Why this is important

- 16 There is a gap in the evidence about parental and healthcare professional
- 17 experience and acceptability of phototherapy. The committee agreed that the
- need for this research should be supported, especially given the greater
- 19 awareness of the crucial importance of close and early skin contact between
- 20 babies and their carers. The study should be a qualitative study in newborn
- 21 babies (term and preterm) with a diagnosis of jaundice but otherwise well.
- 22 Outcomes should include both parental and staff experience, including access
- 23 for bonding and breastfeeding.

24 Update information

- 25 This guideline is an update of NICE guideline CG98 (published May 2010).
- New recommendations have been added for diagnosing jaundice in newborn
- 27 babies.
- 28 These are marked as:

- **[new 2016]** if the evidence has been reviewed and the recommendation
- 2 has been added or updated
- [2016] if the evidence has been reviewed but no change has been made to
- 4 the recommended action.
- 5 New recommendations on treatment were available for consultation in August
- 6 2015. These recommendations are shaded in grey and marked as **[new**
- 7 **2016]**.
- 8 NICE proposes to delete some recommendations from the 2010 guideline.
- 9 because either the evidence has been reviewed and the recommendations
- 10 have been updated, or NICE has updated other relevant guidance and has
- 11 replaced the original recommendations. Recommendations that have been
- 12 <u>deleted or changed</u> sets out these recommendations and includes details of
- 13 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.
- 17 See also the original NICE guideline and supporting documents.

Recommendations that have been deleted or changed 1

2 Recommendations to be deleted

Recommendation in 2010 guideline Comment 1.4.1Use serum bilirubin measurement Replaced with: and the treatment thresholds in the 1.4.1 In babies who have a gestational threshold table and treatment threshold age of 38 weeks or more, who are more graphs[4] when considering the use of than 24 hours old, and who are clinically phototherapy. well: 1.4.2 In babies with a gestational age of Use bilirubin treatment thresholds 38 weeks or more whose bilirubin is in (see the treatment threshold graph in the the 'repeat bilirubin measurement' full guideline) when considering whether category in the threshold table repeat the to use phototherapy or exchange bilirubin measurement in 6-12 hours. transfusion to treat jaundice. 1.4.3 In babies with a gestational age of If serum bilirubin is below the 38 weeks or more whose bilirubin is in phototherapy threshold by less than 50 the 'consider phototherapy' category in micromol/litre, check the record of the threshold table repeat the bilirubin maternal antibodies, ensure that the baby measurement in 6 hours regardless of is feeding adequately and has no signs of whether or not phototherapy has sepsis, and repeat serum bilirubin subsequently been started. measurement as follows: within 18 hours for babies with risk factors for neonatal jaundice (that is, with a sibling who had neonatal jaundice that needed phototherapy or a mother who intends to exclusively breastfeed) within 24 hours for babies without risk factors. [new 2016] 1.4.2 If serum bilirubin is below the phototherapy threshold by more than 50 micromol/litre, do not repeat serum bilirubin measurement unless it is clinically indicated. [new 2016]

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