Consultation Response Form

Document Title: Identification and Management of Neonatal Hypoglycaemia in the Full Term Infant (Birth – 72 hours)
Closing date: 13 June 2023
Please return this form to: **bapm@rcpch.ac.uk**

Comments received on this form will be shared with the BAPM working group to assist with the production of a final version of the document. We will publish the comments received with names attributed on the BAPM website alongside the final published document. Please note that due to the large number of comments received during consultations for BAPM publications we may not be able to respond to all comments on an individual basis.

Dush Batra, Consultant, Nottingham University Hospitals

Page number/ heading / general comments	Line number/ 'general' for comments	Comments Please insert each new comment in a new row.	Response
Executive summary Heading 1	Line 6	Are authors mixed up between the technical definition of fetal growth restriction and 'small for gestational age'. Centile charts technically pick up small/ appropriate/ large for GA. Fetal growth restriction would be more about growth velocity.	It is correct that centile charts will determine those who are SGA. Constitutionally small babies </= 2nd centile are at risk of hypoglycaemia as are larger babies with FGR despite being AGA, who may appear wasted. We have given guidance to help identify babies who may have FGR (>2 centiles discrepancy between OFC and weight) in the absence of sufficient evidence to recommend customised growth charts for detecting pathological fetal growth velocity.

Points 12 and 14		The framework is for first 72 hours and these points go beyond 72 hours. From a practical point of view, guidance is often viewed as a protocol. Many babies will be able to maintain normoglycaemia at less than 150ml/kg/d. If authors still plan to include beyond 72 hours, feed volume up to 150ml/kg/d would be a better suggestion.	We have ensured that throughout the framework recommendations have been kept to the first 72 hours only
Point 19		Dextrose gel should be first choice as is likely to be easily accessible. Teams may spend time getting, checking, double checking Glucagon in a high risk situation and delay treatment.	Either is acceptable but the order has been changed to reflect accessibility.
Point 21		Urine test 'during' hypoglycaemia is impractical. Blood ketones are more useful than urinary ketones. Urine organic acid abnormalities persist if that is the cause of hypoglycaemia.	Most tests are not needed "during" hypoglycaemia and those needed are marked "*" as specified. Advice is for a urine bag to be sited during hypoglycaemia but not to delay treatment.
Point 24		This document is going to be used by MDT. How do authors propose to define 'adequate energy provision'? This should be clear.	We except colleagues to use clinical judgement to determine this since it will be different for different babies and in different situations.
Synposis of supporting evidence	Page 12	Working group suggest dysmorphic features as a potential indication for screening if LGA with features suggestive of BW syndrome. Should that be included in the framework? No maternal Diabetes assumes a perfect world. Too often, gestational diabetes gets missed. Inclusion of LGA has potential of capturing some higher risk babies that get missed.	Babies who are LGA with features of BWS should be screened for hypoglycaemia – this is included in the framework. We are unable to cover missed maternal diagnoses within the remit of this framework.
Flowchart A	Box 1	FGR has changed to IUGR… I would personally suggest using small for gestational age. Flowcharts are often used in isolation. Any abbreviations will need full form for users.	Thank you, IUGR has been changed to FGR. The framework can be used to write local guidelines including adapting the flowchart as required

Vickie Bevan, Neonatal Intensive Care Dietitian, North Bristol NHS Trust

Page number/ heading / general comments	Line number/ 'general' for comments	Comments Please insert each new comment in a new row.	Response
General comment		Please can you reconsider the wording of 'Infants of diabetic mothers' throughout the document. As someone with Type 1 Diabetes I would prefer to be referred to as Infants of mother's with diabetes.	Changed to infants of mothers with diabetes throughout

Page number/ heading / general comments	Line number/ 'general' for comments	Comments Please insert each new comment in a new row.	Response
Executive summary	Point 4	Typing error 'isbecoming'	Thank you, corrected
Executive summary	Point 9	Typing error 'arewell'	Thank you, corrected
Page 9	12	Recommendation 12: No mention of what to do if parents decline the use of formula	This is outside the scope of this document
		Could emphasise more clearly that framework is for babies >37 weeks gestation Specifies "term" in title	≥37+0 has now been included in executive summary
		It is important to distinguish between true congenital hyperinsulinaemia, a rare genetic disorder, and a transient aberrant hyperinsulinaemia, the most common cause of low blood sugar in this group. In our experience, we have found that babies with the latter who undergo 'hypoglycaemia screening' are subsequently fluid restricted in order to give diazoxide, when actually they require an augmentation of nutrition to treat their hypoglycaemia. In such babies, we therefore do not meet their nutritional needs, thus compounding the hypoglycaemia. Performing an early 'hypoglycaemia screen' may therefore not be helpful in the majority of babies who do not actually have a congenital hyperinsulinism.	We agree – most babies will have further testing in consultation with Paediatric Endocrinologists
Page 7	Point 1	Practice point 1 relating to fetal growth restriction and SGA babies. It is worth clarifying that UK-WHO population based centile charts have been used for identifying babies < 2nd centile. I am aware some hospitals use customised growth centile charts (GAP) at birth and identify babies who are at potential risk of hypoglycemia. Is there any evidence for and against use of customised centile charts in identifying potential risk of hypoglycemia ?	Thank you, we agree that the evidence is not sufficient for us to include as strong recommendations.
Page 7	Point 2	Typo 'hasone' to ' has one'	Thank you, corrected
Page 8	Point 5	Is it not that babies with high PCV, also have true low blood glucose results?	Thank you, this has been included in the Appendix
Page 9	Point 13	Can we clarify the reasons please as to the statement that there is no evidence to support the use of donor breast milk	Thank you – this has been clarified

Page 10	Point 16	Typo ‘withhypoglycemia’	Thank you, corrected
Page 10	Point 17	It’s a bit confusing. Are we saying we shouldn’t discharge babies to community until they are at least 24 hrs old or at least 2 sugars > 2 mmol, as both points do not mean the same. Based on the latter, it is still possible to discharge the baby prior to 24 hrs of age.	Thank you, we have clarified this. Babies should be discharged to community only if they have at least 2 sugars > 2 mmol AND are at least 24 hours of age.
Page 10	Point 21	Can we clarify please. are we expecting a newly born baby with BG < 1mmol/l within an hour or two from birth, to have all investigations initiated as per the list? Is it necessary to do even insulin/FFA/ketone bodies for these babies?	Thank you – we agree it is not necessary and have clarified in the framework
Page 11	Point 23	Can we clarify this as transient hyperinsulinism please?	Clinicians would be unable to decide if this was transient or CHI at that point and therefore we refer to hyperinsulinism.
	Point 24	Can we clarify how to say ‘ adequate energy provision’ in a breast fed baby please? Are we saying we calculate glucose load in a fully enterally fed babies as well? Do we need to investigate for HI if the baby’s BG is < 2mmol/l despite being on 8 mg/kg/min glucose load, or their sugars are within normal limits but are needing > 8mg/kg/min glucose load?	This is determined by clinical judgement We do not expect glucose load to be calculate for milk fed babies. These numbers refer to those receiving IV glucose. Yes, in both cases
Page 26	‘Notes’	Typo ‘asan’ Typo ‘innercheek’	Thank you, corrected
Page 27	Appendix 4	Can we also include an example of how to make a specific concentration of glucose please. Example: how to make 12.5% glucose 500 mL bag.	The appendix gives generic instructions that can be adapted as per requirements.

Hannah Brophy, Consultant Neonatologist, Liverpool Neonatal Partnership

Sam Cambridge, Infant Feeding and BFI Project Lead Midwife, Surrey and Sussex Healthcare NHS Trust

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8	13	Can there please be guidance on confirming a low BGL when using hand held monitor? Is it that management should be delayed until a blood gas reading is taken or should management continue as per the reading but the next BGL be a blood gas sample?	Please see Appendix
9	general	'We suggest offering 8-10ml/kg initially.' You state this but this amount is higher than 40-60/kg/day. Is that accurate. Also the flow charts still say 10-15ml/kg. Can you also please clarify that this is not the amount of colostrum expected as it is incredibly rare that any woman is going to be expressing these amounts in the first 24 hours after birth. We are often asked how to support mothers who are only obtaining 0.2mls of colostrum and the expectation is the baby gets the same amount of colostrum as they would have formula.	Thank you, corrected We agree that we do not expect these volumes of colostrum
	General	Can you please clarify the use of NEWTT 2 in regards to this guideline as the scoring and triggers for reluctant feeding and BGL of <2.5 contradict this guideline.	The NEWTT2 guidance has clarified that this does not trigger further glucose monitoring unless in keeping with the hypoglycaemia framework.

Hilary Cruickshank, Physiotherapist, Royal Infirmary of Edinburgh

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General	General	Follow up for these babies is not mentioned. As we know there is a risk for abnormal development it would be good to have some guidance on this. Especially as many units are trying to include them in their follow up services.	Please see p18 practice points 20-21; specific recommendations are outside the remit of the framework.

Sarah Dearman, Co-Chair and Trustee, The Children's Hyperinsulinism Charity

Page number/ heading / general comments	Line number/ 'general' for comments	Comments Please insert each new comment in a new row.	
Page 4 Executive Summary of Recommendations	Point number 2	This should include the need to take a detailed family history to identify if any siblings or parents had a condition, syndrome that could potentially be genetic or pose an 'at risk' factor for hypoglycaemia such as Hyperinsulinism, in these circumstances the baby should be considered 'at risk' and additional monitoring/protocols must be implemented. Medical professionals should not assume that the mother received good pre-natal care and support throughout pregnancy or necessarily attended appointments or reported their own medical concerns or issues, therefore	We agree – and where possible this should be planned in advance of birth - please see p12 We are unable to cover missed maternal diagnoses / aspects of antenatal car within the remit of this framework.

		a detailed history is always essential, to avoid overlooking any potential risk factors.	
Page 7 Framework for Practice Section A: Practice Points	Point number 1	There should not be an over reliance on solely identifying 'at risk' infants from the specific criteria listed: • The Children's Hyperinsulinism Charity 2018 BAPM survey discovered two important findings as to why it is important to remain vigilant to hypoglycaemia on **all** babies and to remain alert to the possibility of hypoglycaemia in babies born to a healthy mother or in a mother who had 'other' complications during pregnancy (see 2): Continued below 1. **74% of mothers described themselves as 'healthy' with no reported concerns or conditions.** 2. Only 1% of mothers had diabetes (type1/2), 5% had gestational diabetes, 4% had a pre-existing medical condition and **16% had 'other' complications such as severe sickness, pre-eclampsia, polyhydramnios (**respondents' parents of a child diagnosed with Congenital Hyperinsulinism)	It is not possible to predict babies who will develop hypoglycaemia in the absence of risk factors. Recognition of the sick newborn is outside the scope of this framework Without risk factors it is inappropriate to test well babies for hypoglycaemia
Page 7 Framework for Practice Section A: Practice Points	Point number 2 and Flowcharts A and B	add 'breathing difficulties' and 'jitteriness' to the list.	Jitteriness by itself is common and not a reason to measure blood glucose
Page 7 Framework for Practice Section A: Practice Points	Point Number 2 Final paragraph	we would strongly argue against the finding that 'jitteriness' on its own is not an indication to take a blood glucose measurement. In our survey where we asked 'how did your child present before hypoglycaemia was confirmed' 16% reported jitteriness this was just one percent less than the leading symptom of poor feeding and higher than the other signs and symptoms identified and listed as warranting a blood glucose measurement i.e. seizures 13%, hypotonia 11%, cyanosis 8% we therefore assert that jitteriness should warrant a blood glucose measurement. Parental feedback "***Dr was just about to discharge my daughter even though she was jittering. We asked for a blood sugar test to be done which he reluctantly did, her level was 0.9 mmol/l".***	We disagree; jitteriness is common and therefore likely to be reported in babies both with and without hypoglycaemia

Page 8 point 7 – 'how the likelihood of hypoglycaemia can be minimised' and Patient information Leaflet	Page 8 point 7 and Page 21 Patient Info Leaflet	Patient Information Sheet Recommendations (page 21) to: ***Feed as often as possible in the first few days,*** ***Feed for as long, or as much, as your baby wants, Feed as often as baby wants*** Needs to be more certain, on full term infants when should this advice continue to? It is unclear if it is a 'few days' and what that means to a parent. There is a clear risk that reliance on this advice for a prolonged period could mask hypoglycaemia. **There needs to be a far greater emphasis on the transition of routine** i.e. to be vigilant at the time of 'stretching' out any feeds or allowing a baby to sleep for longer periods (e.g the advice that it is no longer required to wake a baby every 2-3 hours) At this extremely vulnerable transition time – hypervigilance of the signs and symptoms of hypoglycaemia should be considered and any concerns are reported without delay. This relies on good quality patient information and for all medical professionals to understand that a quick discharge from hospital under 24 hours can increase the risk of hypoglycaemia occurring in the home. Our survey found that whilst 68% of babies with Hyperinsulinism presented with hypoglycaemia in the first 24 hours of birth a significant number 16% presented during the first **7 days of birth** and this should be viewed as a window of time when there is an increased risk and need for parents to be vigilant to the signs and symptoms of hypoglycaemia in babies at home. This is particularly true, of babies who may have been slow feeders and the gap between feeds was non-existent or limited leading to a real risk of false or misleading blood glucose measurements in the hospital setting. Which may then show itself later in the home and particularly at a time of transition as described above. Extremely important to encourage parents to report if something 'just doesn't seem right' about their baby as it is important to note that they may not display the listed signs and symptoms of hypoglycaemia or they may be asymptomatic, but often the parent has detected the feeling something is not right, and this should not be	The Parent information Leaflet has been reworded The framework recommends that babies at risk of hypoglycaemia remain in hospital for at least 24 hours Management beyond 72 hours is outside the scope of this framework

		dismissed (see parental comments at end of document) again an alert on the baby could help medical professionals to consider hypoglycaemia if the baby presents at a later date, with unexplained or non-specific symptoms. As well as ensuring that the time of stretching out feeds/longer sleep times is queried as a potential trigger to an underlying cause of hypoglycaemia and blood glucose measurements are taken.	
Page 20 Patient Information Leaflet	Pages 20 -23	The patient leaflet feels incredibly complacent and falsely reassuring particularly in the case of quick discharges (24 hours) with 'once you are home no special care is needed' and to follow the advice for all new-born babies. it is inexplicable why the leaflet advises to look for signs that your baby is well? Assuming it means unwell? The NHS website is often the first point of call for parents and particularly as it is often encouraged – **it is important that the website is updated <u>urgently</u> with appropriate guidance on hypoglycaemia in babies** the attached update document was produced by Hyperinsulinism Specialist Teams and The Children's Hyperinsulinism Charity and subsequently approved by NHSE but has not been uploaded/updated. Current NHS website advice is inappropriate e.g. treat with jelly babies, sugary drinks. It is unclear why parents of babies who have displayed hypoglycaemia on wards are not afforded an alert system so any call for an ambulance or trip to A&E would alert the medical professional of the earlier incident of hypoglycaemia, provided clear information on the signs and symptoms of hypoglycaemia and given more advice as to any transitional changes in feeding and noticing any concerns. It is essential there is more clarification around feeding concerns and what to do if feeding issues persist at home. **The Children's Hyperinsulinism Charity would strongly recommend a follow up blood glucose test on babies who were found to have incidents of hypoglycaemia and subsequently discharged at the 5 day heel prick test as part of routine.**	The Parent information Leaflet has been reworded We agree that the information on the NHS website is not relevant to newborn babies but are unable to make changes to it (but we are pleased that you have already requested changes which have been approved by NHSE) How individual hospitals arrange access to paediatric services is a local issue and outside the remit of this FfP. We disagree; there is no evidence that this is beneficial and as your survey found the vast majority of children who presented with later hypoglycaemia had not had episodes of hypoglycaemia in the first 24 hours.

Page 12 SECTION B: Synopsis of supporting evidence	Page 12 last paragraph on page	in the case of Hyperinsulinism it should **always** be necessary to screen.	We agree – and where possible this should be planned in advance of birth - (the reference to occasional is the frequency of the situation not the action)
BAPM Framework Flow Charts	Where the framework states 'pre-feed blood glucose measurements'	**Advice in the BAPM document including Flowcharts must take account of 'slow feeders' with parents reporting that one 'scheduled' feed ran into the next and/or was finished with NG tubes. This meant that scheduled 'pre-feed' blood glucose measurements were falsely reassuring and misleading, as there simply wasn't a gap between feeds. Pre-feed needs to have a warning to specifically record when the last feed completed, in order that they are truly considered to be a pre-feed blood glucose and post-feed.**	This has been incorporated
Patient Information Leaflet	Pages 20-24	The Patient Information Leaflet is not detailed enough, it should have a list of the signs and symptoms of hypoglycaemia in babies. Also, it should detail what symptoms warrant urgent action – we would therefore make a strong **Recommendation to follow the guidance in the Institute of Health Visitors parent tips on hypoglycaemia** written with Hyperinsulinism Specialist Teams and The Children's Hyperinsulinism Charity which advises on signs and symptoms and NHS 111 action on steps to take in event of hypoglycaemia which details signs and symptoms and action to take: https://ihv.org.uk/news-and-views/news/updated-parent-tip-hypoglycaemia/	The Parent information Leaflet has been reworded
Flowcharts	Flowcharts	Fast discharge (24 hours) leads to increased risk of hypoglycaemia in the home, particularly when 16% of respondents to our survey stated their child present with hypoglycaemia **after 24 hours and before 7 days.**	Most women and babies are discharge before 24 hours which is not considered fast and there is no evidence that it leads to increased risk of hypoglycaemia in the absence of risk factors. It is currently impossible to predict babies with CHI in the absence of risk factors or to identify / manage them in any other way at present.
Page 11 Persistent low blood glucose measurement	Page 11 Point 25	**Where the suspected or established cause is Hyperinsulinism there should be one recommended blood glucose threshold measurement of 3.5 and not confused by two measurements of 3.0mmol. 3.5mmol/l is**	Health professionals involved with caring for newborn babies are well versed in changes which occur following birth and at different gestational ages so it is appropriate to use different

		supported by families who recognise the seriousness of Hyperinsulinism on the developing brain. The absence of alternative protection to the brain in hyperinsulinism makes it particularly vulnerable and as such 3.5mmol/l is considered to be the right threshold level by families.	thresholds at different ages and for different clinical conditions. The treatment thresholds for babies with suspected hyperinsulinism < and >48 hours are supported by paediatric endocrinologists.

Maria Salomon Estebanez, Consultant Paediatric Endocrinologist, Royal Manchester Children's Hospital

Please find attached Consultation Response Form on behalf of the Congenital Hyperinsulinism Leads from Royal Manchester Children's Hospital (Dr Salomon Estebanez and Professor Banerjee), Alder Hey Children's Hospital (Dr Didi and Dr Senniappan) and Great Ormond Street Children's Hospital (Dr Dastamani), regarding the framework " Identification and Management of Neonatal Hypoglycaemia in the Full Term Infant (birth - 72 hours)".

Page number/ heading / general comments	**Line number/ 'general' for comments**	**Comments** **Please insert each new comment in a new row.**	
Executive Summary	Point 8	"Persistent hypoglycaemia (> 2 measurements < 2.0 mmol/L in the first 48 hours) requires urgent medical review and investigations". This recommendation is difficult to follow if guided by this framework as a lot of babies, even with risk factors, are discharged from hospital in the 24 hours of life. Hence, the two blood glucose measurements recommended (before the second feed - at 2-4 hours of life - and before the third feed – before 8 hours of life-) are too early and could miss hypoglycaemia after the first 8 hours of age, particularly if discharged at 24 hours of life or earlier	The framework recommends that babies with risk factors for hypoglycaemia are kept in hospital for at least 24 hours.
Page 7		Babies that are large for gestation age should be included as a risk factor for persistent hypoglycaemia – undiagnosed maternal diabetes could cause large for gestational age babies and persistent hypoglycaemia, which could be missed if not in the risk factor group. Similarly, babies with some genetic forms of congenital hyperinsulinism are typically large for gestational age, as well as babies with Beckwith-Wiedemann syndrome , who are macrosomic and do not always have clear dysmorphic features.	We disagree, there is insufficient evidence to recommend screening of LGA babies in the absence of maternal diabetes. We are unable to cover missed maternal diagnoses within the remit of this framework. Babies who are LGA with features of BWS (eg macrosomia) should be screened for hypoglycaemia – this is included in the framework.

		Newborns with family history of genetic CHI (in siblings or parents) should also be screened for hypoglycaemia.	We agree – and where possible this should be planned in advance of birth - please see p12
Page 9	General point 14	How to ensure that glucose remains > 2.0 mmol/L, even if it has been > 2 mmol/L in the first 8 hours of life, it could drop further to < 2.0 in the first 48-72 hours, especially if "feeding responsively"	The framework recommends maintaining clinical vigilance as well as observing feeding.
Page 11	Point 25	Whilst awaiting specialist input in cases with suspected or confirmed hyperinsulinism, this framework should not be used (rather than should be used with caution) if a baby is > 72 hours. And hypoglycaemia threshold should be raised to 3.5 mmol/L.	We have clarified the framework is for use in the first 72 hours and have emphasised the change in treatment threshold from 3.0mmol/L <48 hours of age and 3.5mmol/L from 48 hours in babies with suspected hyperinsulinism
Page 12	islet cell adenoma	Not sure what this refers to, but extremely rare in newborns and should be removed.	Removed
Page 14	Last para	Why are other infants with risk factors considered different to infants of diabetic mother? Does this imply that other infants with risk factors could potentially be discharged at 12 hours if 2 consecutive blood glucose measurements > 2 mmol/L and effective breastfeeding has been established? How can effective breastfeeding be established within or before the first 24 hours of life?	This has been reworded to avoid confusion
Page 18	diagnostic clues for hypopituitarism	rather than skin hyperpigmentation in FGD - midline defects, undescended testes or micropenis could be included as diagnostic clues for hypopituitarism	Thank you, amended
Flowchart C	*	* if GIR > 8 mg/kg/min, test for hyperinsulinism – this should have been tested at the time of the hyposcreen. It should be changed to: if GIR is > 8 mg/kg/min, suspect hyperinsulinism, contact specialist team and increase the glucose threshold to 3.5 mmol/L.	Thank you, amended

Nigel Gooding, Consultant Pharmacist – Neonates & Paediatrics, Cambridge University Hospitals NHS Foundation Trust

<table>
<tr><th>Page number/ heading / general comments</th><th>Line number/ 'general' for comments</th><th>Comments

Please insert each new comment in a new row.</th><th></th></tr>
<tr><td>General comments</td><td>General</td><td>Throughout the document Glucose gel is referred to as 'Dextrose' gel. Please could this be changed to say Glucose 40% oral gel as the BNFC and product literature use the term glucose 40% oral gel.</td><td>Thank you – changed where appropriate</td></tr>
<tr><td>Page 10.</td><td>Points 18 and 19</td><td>Where glucose 40% oral gel is mentioned. After dose of 200mg/kg, suggest adding refer to appendix 3 for weight banded doses.</td><td>Appendix 3 referenced</td></tr>
<tr><td>Page 26 (appendix 3)</td><td>Dose section</td><td>Suggest removing 'If a weight per weight preparation of 40% dextrose gel is used, practitioners should be aware of the weight of 1ml of the preparation and calculate the ml/kg volume required to deliver 200mg/kg of dextrose. Advice from the local pharmacist is recommended'.
Replace with 'Glucose 40% oral gel contains approximately 400mg/ml of glucose. A dose of 200mg/kg is approximately equivalent to 0.5ml/kg.
The following table provides a practical volume to administer the 200mg/kg/dose for babies within specific weight bands.
<table><tr><td>Weight of baby (kg)</td><td>Volume of gel (ml)</td><td>Dose (mg)</td></tr><tr><td>1.5 – 1.99 kg</td><td>1ml</td><td>400mg</td></tr><tr><td>2.0 – 2.99 kg</td><td>1.5ml</td><td>600mg</td></tr><tr><td>3.0 – 3.99 kg</td><td>2ml</td><td>800mg</td></tr><tr><td>4.0 – 4.99 kg</td><td>2.5ml</td><td>1000mg</td></tr><tr><td>5.0 – 5.99 kg</td><td>3ml</td><td>1200mg</td></tr><tr><td>6.0 – 6.99 kg</td><td>3.5ml</td><td>1400mg</td></tr></table>
Suggest adding this dose table with weight banded doses. Many centres use a table like this and it makes calculation of the dose and volume much easier.</td><td>Updated</td></tr>
<tr><td>Page 27 (appendix 4)</td><td>How to make up any concentration of glucose</td><td>We felt that the calculation method was quite complex. It might be easier to add a table like this instead (or in addition). In some cases these will only be approximately the actual desired concentration, but should be clinically insignificant.
<table><tr><td></td><td colspan="2">PREPARING 500ML BAGS</td></tr><tr><td rowspan="2">% Glucose solution required</td><td colspan="2">Combination of glucose solutions required</td></tr><tr><td>10% Glucose</td><td>50% Glucose</td></tr></table></td><td>Thank you. Due to the difference in local practices this has not been</td></tr>
</table>

				(to add to 500ml glucose bag once equivalent volume has already been removed from bag)		included but a note made that neonatal units may wish to include similar in their guidance.
			12.5%	470ml (remove 30ml from 500ml bag)	30ml	
			15%	440ml (remove 60ml from 500ml bag)	60ml	
			17.5%	405ml (remove 95ml from 500ml bag	95ml	
			20%	375ml (remove 125ml from 500ml bag)	125ml	
			25%	310ml (remove 190ml from 500ml bag)	190ml	
			30%	250ml (remove 250ml from 500ml bag)	250ml	
			Please note that once prepared some concentrations will only be approximately the actual desired concentration, due to variation in bag overages and volumes used.			
		If a more accurate way is required then the table below is used at Evelina Hospital (but volumes included are not as easy to measure as in the table above).				

<table>
<tr>
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<td>
<h2>Preparation of glucose 12.5%, 15%, 17.5% and, 25% solutions</h2>
Non-commercialised glucose concentrations can be prepared on the ward by adding glucose 50% to a standard 500mL bag of glucose 10%.
Use the table below to achieve the desired concentration.
<table>
<tr><th>Volume to remove from glucose 10% bag</th><th>Volume of glucose50% to add to bag</th><th>Final concentration</th><th>Final volume</th></tr>
<tr><td>31.25mL</td><td>31.25mL</td><td>12.5%</td><td>500mL</td></tr>
<tr><td>62.5mL</td><td>62.5mL</td><td>15%</td><td>500mL</td></tr>
<tr><td>93.75mL</td><td>93.75mL</td><td>17.5%</td><td>500mL</td></tr>
<tr><td>187.5mL</td><td>187.5mL</td><td>25%</td><td>500mL</td></tr>
</table>
Mix well.
If the calculation instructions remain in the document, then we would suggest adding a worked example as well.
</td>
<td></td>
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<tr>
<td>Page 35 & 36</td>
<td>Flowchart B and C</td>
<td>Where administration of 40% dextrose gel 200mg/kg is stated in the flowsheets, suggest referring to dosing table in appendix 3, if decision is made to include our suggestion of adding the weight banded dose table.</td>
<td>Appendix referenced</td>
</tr>
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Sophie Harvey, Infant Feeding Coordinator, Norfolk and Norwich University Hospital

Page number/ heading / general comments	Line number/ 'general' for comments	Comments Please insert each new comment in a new row.	
9 / 13	There is no evidence to support the use of donor breastmilk as part of a hypoglycaemia pathway in the term population.	I feel this statement should be removed in its entirety until evidence is available to support the use of donor human milk as part of the hypoglycaemia pathway for term infants. The current statement is unnecessary and can be viewed negatively towards the use of donor human milk for term infants. I feel this statement will deter units from providing donor human milk for babies at risk of hypoglycaemia. In the absence of maternal breastmilk, the options for supplementation should be donor human milk or formula. If the statement says there is no evidence to support the use of donor human milk, then parents will not be offered a choice regarding supplementation type.	Edited to reflect lack of evidence either way

Lucy Lowe, Infant Feeding Specialist, Norfolk and Norwich University Hospital

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9 / 13	There is no evidence to support the use of donor breastmilk as part of a hypoglycaemia pathway in the term population.	There is no evidence to refute the use of donor human milk as part of the hypoglycaemia pathway for term infants, therefore this statement is not needed and projects the message that donor human milk is of no value. The statement risks professionals and families alike from not instigating the use of donor milk where supplementation is required, not just for those at risk of hypoglycaemia. Where mothers own milk is unavailable, donor milk is the next best option for neonates (Who Health Organisation). Statement 13 of the BAPM draft document risks being interpreted as "do not give donor milk - use formula as this is the appropriate/superior option for supplementation". Research shows us that this is not the case and that, in fact, early formula supplementation reduces maternal confidence in breastfeeding (Hinic, 2016), reduces duration of breastfeeding (Academy of Breastfeeding Medicine, 2017) and consequently negatively impacts on the long term health of both mother and baby (Bartick et al, 2016; Walker, 2015). In contrast, donor milk use for supplementation is shown to have a positive effect in supporting the mental health and wellbeing of mothers (Brown and Shenker, 2022). The appropriate introduction and use of donor human milk has been repeatedly shown to increase maternal breastfeeding rates on discharge (Kantorowska et al. 2016, Abhisavam et al. 2017).	Edited to reflect lack of evidence either way

Kathryn Macallister, Neonatal Registrar, St Michael's Hospital, Bristol

Page number/ heading / general comments	Line number/ 'general' for comments	Comments Please insert each new comment in a new row.	
Page 4	Point 6	Thank you for all your hard work on this framework. I wonder if you could just clarify what intervention is needed if a well baby with risk factors has a blood glucose of 1.0-1.9 which remains 1.0-1.9 at the next measurement? You mention that an operational threshold approach should be used to guide interventions in such babies on page 4, but throughout the rest of the framework I cannot find mention of how these specific babies should be managed differently, only that once babies have had MORE than two measurements in this range they should be reviewed and investigated. Otherwise flowchart B implies that if glucose is 1.0-1.9 before the second feed and remains 1.0-1.9 before the next feed then these babies can still go round the 'loop' again before moving to box 3.	They could receive glucose 40% oral gel (via buccal route) and should be fed, they should have a further pre-feed BG prior to the next feed (which should not be more than 3 hours after the start of the last feed); a further BG measurement <2.0mmol/L would necessitate investigation and treatment.

Gillian Meldrum, Baby Friendly / Infant Feeding Lead Midwife

Page number/ heading / general comments	Line number/ 'general' for comments	Comments Please insert each new comment in a new row.	
Whole doc	General	Numerous instances of missed space between words – just needs spell / grammar checking.	Thank you – there was a formatting issue following document upload

P1	Title	Although the title is '(birth – 72 hours)' there is little (I couldn't find anything) in the FfP which refers to care of babies 24-72h old, other than indirectly in the final point in the parents' leaflet that refers to checking their baby is well when they go home. Some of the litigation cases occurred at home on days 2-3. I think it is important that staff understand that once the BG tests have been completed, the baby is still at risk for HG, and monitoring feeds and wellbeing is still paramount – by parents and/or staff. In my experience, there is a big focus on the blood tests, and once they are both OK (at 4-8h of age) there are minimal ongoing concerns. Guidance on ongoing monitoring is mentioned for up to 24h, but it needs to be highlighted more clearly. I would suggest that the point that babies can experience clinically significant HG on days 2 & 3 is made more clear.	Thank you; we have emphasised ongoing assessment
P4	Point 3	OFC – please explain	Expanded
P4	Point 9	'Practitioners need skills to distinguish between infants with abnormal feeding behaviours that can occur with other signs to suggest illness, and infants who arewell but reluctant to feed.' I would suggest that the FfP should provide the knowledge to allow practitioners to distinguish – otherwise, what specific skills are we talking about? How can they be acquired?	This is outside the scope of the FfP
P8	L1-3	Abnormal feeding behaviour needs much clearer definitions – I would say that all these criteria can be within the range of 'normal' feeding behaviours. Not waking for feeds – so what frequency of waking for feeds is 'normal' or 'abnormal'? How often is 'very frequent'? – we are encouraging little and often, so I don't know what would be abnormally frequent. Not sucking effectively – this phrase can be used to describe vigorous sucking with a shallow latch when milk is not being transferred effectively – but I think the intention is to describe a baby with an inability to suck or what is often described as a 'weak suck'.	In depth descriptions of feeding is beyond the remit of this FfP.

		Appearing unsettled – again, how unsettled would it have to be? Why is it 'appearing' unsettled rather than simply 'unsettled'? Unsettled for how long? Especially after a period of feeding well – I agree with this criteria, and would suggest it is given more emphasis, not just as a final phrase in a long sentence. What factors should be 'considered' when making a decision to do BG test or not? Staff need guidance on this, otherwise it may be understood that a BG test is recommended. P14 Line 8 ref 3 cited with ref to 'abnormal feeding behaviours, which may be a presenting sign of significant HG' – this ref is the litigation series which relates to cases of prolonged ineffective feeding but I don't think it is with reference to the first 4-6 hours after birth. If observations, BG tests and at least 3 hourly feeds are achieved in the 4-6 hours time frame, then any subsequent 'abnormal feeding' would be of concern.	This section has been restructured.
P8	Para 12 L9	Clear guidance very welcome, but what is the evidence base for the volumes of formula recommended? Can they be included in the references please? (40-60ml/kg/per day during the first 24 hours; 70-90 ml/kg/per day 24-48 hours; 100-120 ml/kg/per day 48-72 hours; 150/ml/kg/per day beyond this) P14 'We suggest starting with 8-10ml/kg/feed' refers to reference 34 – but this reference is about obese mothers, and doesn't seem relevant to me – may be a mistake.	Where evidence is lacking and recommendation is required the working group relied on consensus of expertise Amended
P9	Point 11	'Offer the breast in response to feeding cues but with intervals of no longer than three hours from the beginning of the last feed' Can I just clarify this point – so this seems to say the baby should be offered a feed rather than achieve a feed within 3 hours of start of previous feed? I think this is confusing – a baby can take hours from being offered a feed to taking a feed. I think what is intended is that the feeds should take place 3 hourly (from beginning of previous feed) – isn't it? This links to my comment below re P21 L8.	This has been expanded in practice point 2

P11	Para 26 L8	As above, p8 L1-3 – how can midwives distiniguish whether feeding behaviours reflect an abnormal clinical state or not? Are there any objective criteria beyond abnormal clinical observations, or parental concerns? There are other references to 'skilled' assessment in the document – where I think what is needed is information.	Practitioners need to be skilled in assessing abnormal feeding behaviours. We proposed a practical definition. The assessment needs to be interpreted in the context of previous feeding and other clinical signs.
P11	Para 27	This is very clear – compare to para 26 comments above	
P14	L9	'Thorough clinical assessment cannot be made effectively during sleep.' So what assessment should be carried out on a sleeping baby? I would suggest a sleeping baby should be picked up and handled to assess tone and stimulated to assess responsiveness (see parents' leaflet).	~~In depth discussions about feeding behaviour is beyond the remit of this FfP. Practitioners need to be skilled in assessing abnormal feeding behaviours. We proposed a practical definition. The assessment needs to be interpreted in the context of previous feeding and other clinical signs.~~
P14	L27	'If the infant is not showing any feeding cues within four hours, then this should be considered a sign of possible hypoglycaemia and should prompt BG measurement.' Is this with reference to babies on the HG pathway? They will be having a BG test at 3-4 hours anyway, including if they are showing feeding cues – so is this in reference to babies not at increased risk for HG? Or is it in reference to after the blood tests have been done, and following previous effective feeding? Please clarify.	Babies on the pathway should indeed be having their BG measured at this time irrespective of exhibiting feeding cues; the purpose of the statement is to prompt BG measurement even if the baby isn't showing signs feeding cues in case the reader is tempted to delay BG measurement until cues are exhibited (risking longer time period to elapse)
P21	L8	'start to offer a feed about 3 hours after the start of the previous feed.' If we want babies to feed at intervals of no more than 3 hours from the start of one feed to the start of the next feed, 3 hours is a bit late to start – this is likely to lead to feelings of pressure on the part of mother and staff – as the baby NEEDS to feed immediately. So if we want to promote an unhurried approach, with lots of stimulation of instinctive feeding behaviours, START to offer at 2 hours seems more sensible – so you can have an hour of unhurried skin contact and cuddling before the pressure is on.	Agree; the information leaflet has been amended This FfP is not aimed at the preterm baby

		(We know that prem babies feed more effectively after 20mins of parents talking to them prior to feed.)	
P21	L11	How about adding in: If you are reading this leaflet before your baby is born, you may want to try expressing your colostrum before the birth, so you can learn how to do it – and you may get some colostrum to keep in reserve if needed. Talk to your midwife about how to do this.	Agree; the information leaflet has been amended
P22	L8	'Look at the colour of your baby's lips and tongue' I would suggest 'baby's inner lips' as more inclusive of dark skin tone.	Agree; the information leaflet has been amended
P22	L22	'have' skin to skin contact instead of 'provide'	Thank you
P22	L30	Could add: Sometimes a small amount of colostrum or formula will stimulate your baby to be more ready and able to feed at the breast. Briefly offer the breast again after a small feed, and see what happens.	Thank you
P22	L33	'If you are breastfeeding and advised to give some infant formula' I suggest 'advised to give some expressed colostrum or formula' to avoid prolonged EBM feeding.	Thank you; the information leaflet has been amended
P24	L29	I don't understand what 'assisted feeding methods' means, which can result in feeding cues.	
P25	L21	Include deep rhythmic sucking with pauses (and/or swallows?)?	Thank you; the information leaflet has been amended

Rachel Mills, Infant Feeding Coordinator, Powys Teaching Health Board

Page number/ heading / general comments	Line number/ 'general' for comments	Comments Please insert each new comment in a new row.	
General	General	There is nothing included, around the management of an at risk of hypoglycaemia baby that is born at home or within a community setting in a planned or an unplanned situation. The previous guideline recommended giving a bolus of glucose gel as a safety net to support thermoregulation on transfer in an ambulance setting and for baby to be commenced on the hypo pathway on admission to the PN ward at the nearest DGH. I would welcome your response regarding this issue.	Outside remit

Janka Nixon, Saving Babies Lives Care Bundle Specialist Midwife

Page number/ heading / general comments	Line number/ 'general' for comments	Comments Please insert each new comment in a new row.	
P7/Identification of infants at risk of impaired metabolic adaptation and recognition of clinical signs		One of my main concerns is that many maternity units are using 2 different postnatal system to identify babies who are either small or large for gestation age. Many maternity settings are using GAP protocol to identify SGA/IUGR babies during antenatal period and then customise birth weight centile once the baby is born, however if the baby is needing neonatal input the birth weight centile is determined using WHO chart, which are inflexible and does not take into consideration maternal	FGR should be defined as ≤2nd centile using the gestation and sex specific growth chart. At present there is insufficient evidence to recommend the use of customised growth charts for detection of infants at risk of hypoglycaemia, and clinical assessment of FGR at birth remains important.

		characteristics. This often causes confusion amongst the health professionals. Maternal characteristics play a crucial role in determining if the baby is SGA, average or LGA. Although, weight-based risk factors for a metabolic condition such as hypoglycaemia depends on baby's lean body mass, fat reserves to maintain gluconeogenesis during transitional phase after birth, if the baby is constitutionally small and not IUGR these reserves will be present, and treatment would not be required. With customised birthweight centile, the centile changes depending on how high the mother is, ethnic origin, BMI whereas with WHO charts centile remains the same for all the babies born at the same gestational age. This can lead to missing or overtreating babies. Please see attached examples.	Disagree, SGA remains a risk factor for hypoglycaemia and there is not the evidence to recommend use of other factors to determine babies who are not at risk of hypoglycaemia.

Dr Ozioma Obi, Neonatal Consultant, University Hospital Lewisham

My main request is for clarification as follows please. We would be extremely grateful for this to be included in the final draft:

Page number/ heading / general comments	Line number/ 'general' for comments	Comments	
		Thank you for all of the hard work that has gone into producing this document, both from the original authors and the reviewing team.	Thank you

P8		Section 4. Paragraph 2, Line 8 – request to define the term "low values" please We have found that this can be a point of individual interpretation leading to some interpreting the guidance in this paragraph as: If a handheld glucometer is used, ***"low values = values on handheld glucometer reading less than 2.6mmols" should be confirmed using an accurate method*** so that assignment to the correct clinical pathway can be made. And others interpreting the guidance in this paragraph as: If a handheld glucometer is used, ***"low values = values on handheld glucometer reading less than 2.0mmols" should be confirmed using an accurate method*** so that assignment to the correct clinical pathway can be made.	This will depend on the specific glucometer and manufacturers recommendations; specific advice about confirmatory tests are outside the remit of the FfP but guidance has been given about use of POCT

		We would be grateful for some clarity please on the intention of the authors when stating "low values" and therefore at what level confirmation using an accurate method is required. I feel that it would be very helpful and important to clarify please, as to remain as "low values" has left this open to interpretation to be essentially any chosen value threshold that one would define as "low".	
P13		Paragraph 3, Line 6 – may need a space after the "%" sign	Thank you
P13		Paragraph 3, Line 7 – is this meant to read **+/-** 0.83mmols/L? (i.e. plus or minus)	Agree, this is the correct interpretation
P13		Paragraph 4, Line 2 – request to define the term "low values" please (Full details as per the p8 comment in full)	As before
P23		Paragraph 1, Line 1 – suggest a space between words "your" and "baby's"	Thank you, amended
P23		Paragraph 2, Line 3 – suggest a space between words "you" and "and"	Thank you, amended
P23		Paragraph 3, Line 1 – suggest a space between words "and" and "most"	Thank you, amended
P23		Paragraph 4, Line 2 – suggest a space between words "particular" and "reason"	Thank you, amended
P23		Paragraph 5, Line 1 – suggest a space between words "when" and "he"	Thank you, amended
P23		Paragraph 6, Line 2 – suggest a space between words "worried" and "at"	Thank you, amended

P24		Paragraph 3, Line 1 – suggest a space between words "spoon" and "or"	Thank you, amended
P25		Paragraph 2 title – "If the mother does not want to hand express" Paragraph 3 title – "If the mother chooses not to express colostrum" – seems to be duplication – is it worth combining the 2 sections?	Agree; the information leaflet has been amended
P34		Flowchart A: title – Would suggest changing the title of Flowchart A from: "Management from birth – 48 hours of infants (≥ 37 weeks) at risk of hypoglycaemia" To: "Management from birth – **72** hours **for** infants at risk of hypoglycaemia" to align more with the guidance document title	Title has been changed to reflect time period of use
P34		Flowchart A: Box 1 Line 4, small typo – should read "2nd " rather than 2rd and would suggest a space between words "age" and "and"	Thank you, amended
P34		Flowchart A: Blue box – suggest a space between words "second" and "feed"	Thank you, amended
P37		Flowchart D: Blue box Line 2– suggest a space between words "to" and "skin" Line 3 – suggest a space between words "hr" and "or" Line 7 – suggest a space between words "readiness" and "to" Line 13 – suggest a space between words "give" and "formula"	Thank you, amended
		Please could you include any guidance on further management when baby has been found to have low blood sugars on incidental finding, (eg blood gas as a repeat of an abnormal cord gas) prior to a first feed – I'm inclined to this that this result should probably be disregarded, and the usual process followed. I feel that this might avoid the value being responded to. (This may differ on a case by case basis).	BG measurement should be performed in babies who have evidence of perinatal acidosis as they too are at risk of hypoglycaemia and should prompt clinical review and intervention as necessary.

Sarah Paxman, Neonatal Quality Improvement Lead, Suffolk and North East Essex

Page number/ heading / general comments	Line number/ 'general' for comments	Comments Please insert each new comment in a new row.	
	General	I wonder if there has been any discussion at BAPM about using a statement of inclusivity at the beginning of guidelines? The key words in this document appear to be breastfeeding / breastmilk / mothers, etc. (which can be 'chestfeeding', 'human milk' or 'birthing person' etc etc to those who do not identify as women. We are doing some work on this within our LMNS and have made a decision to use additive inclusive language, i.e. 'women and birthing people' / use statements of inclusivity to keep things simple in the wording of guidelines.	Thank you, this has been addressed
5		There is reference to the first 48-72 hours twice on this page. Just thinking this could simply read 'the first 72 hours' .	Thank you; 48-72 hours reflects the aim of the FfP to cover the period of metabolic transition
	General	The content of Appendix 1 is so useful, and it would be great if this was more widely used. I wonder if it would be possible to make it a bit more eye-catching and easy to read. Perhaps there could be a separate BAPM leaflet template on the BAPM website for teams to download and add their own Trust logo? This would be really helpful and save a lot of teams time and resources, whilst improving the quality of information to parents.	Agree – we will make this suggestion to BAPM
	General	Just noticed a lot of words have no spaces between them – you are probably already aware!	Thank you – there was a formatting issue following uploading
10 & 26	Appendix 3	Just a comment – thank you so much for clarifying that oral dextrose can be given as an interim measure while arranging urgent medical review and treatment with IV Glucose. This has been a point of confusion at local level in the past when investigating incidents where treatment was delayed.	Thank you
		Hope this is helpful – intending to try and make a positive contribution, rather than be a nit-picker! Thanks for all the work you do.	Thank you

David Quine, Neonatal Consultant, Royal Infirmary Edinburgh

Page number/ heading / general comments	Line number/ 'general' for comments	Comments Please insert each new comment in a new row.	
General	General	Many thanks for this updated guidance to standardise the investigation and management of Hypoglycaemia. One of the biggest changes I note is the change in title and coverage period from 48 hours to 72 hours, I have several comments on this: 1) Your guidance appears to be very focused on management up to admission, but has limited guidance on weaning up on iv fluids and weaning back down again, supporting ongoing feeds and reducing feed intervals or spacing out again. 2) Your flow charts still mention 48 hours, and do not seem to cover 48-72 hours. 3) Flowcharts A and B really only go up to 24 hours, and have no information about weaning up on feed volumes, reducing feed interval or spacing this out again. Some addition guidance in all these areas would be welcomed.	Agree; the purpose of covering the first 72 hours reflects the aim of the FfP to cover the period of metabolic transition, providing information relevant to this timeframe. See Flowchart C. Detailed management of babies on neonatal units receiving i.v. fluids is outside the remit. Information is given on feeding and flowchart C is relevant throughout the first 72 hours
General	General	Your practice points and Section B: Synopsis of supporting evidence appear to have become mixed up, have you added a practice point somewhere but not changed the supporting evidence section ? You have 27 practice points but only quote evidence for 26.	Thank you; amended
Page 10	Practice point 21	The threshold for further investigation of Hypoglycaemia still feels excessive, in practice we know many of these tests would not be back or really influence the transient nature of many of these infants low sugars. Has any literature review suggested otherwise ? Do we know what percentage of infants this changes the management significantly ? How many of these infants will go home with glucose monitoring or a formal diagnosis of HI ? Would this fit the Wilson criteria for a screening test for HI ? If left at this threshold, consider including normal values for these tests, my experience has been these are chased after discharge by junior	Outside remit Reference values will vary between laboratories

		doctors with high risk of misinterpreting the results. If there isn't normative data on these tests one has to ask why are we doing them ?	
Page 11	Practice point 22	Should this be "one or two measurements of 1.0-1.9"-this is in keeping with other statements including practice point 23	Thank you; amended
Page 11	Practice point 25	I and colleagues are extremely concerned the high sugar thresholds quoted in practice point 25, from a very early stage (48 hours or even 72 if that is meant to be the case) are leading clinicians to escalate treatments in otherwise healthy infants with transient low glucose levels, causing untold harm to families through longer hospital stays, reduced breast feeding and family disharmony, when we have so little evidence that this firstly causes harm or can be influenced by the strategies you outline. (Ref A) "We could define Hypoglycaemia as a statistically low glucose, as a glucose which causes short term CNS dysfunction, or as a glucose level which causes permanent CNS injury, or as a blood glucose level below which treatment improves outcomes. It seems unlikely that there is a single threshold that applies to all these potential definitions" (ref B) You appear to be basing your 48-72 hour threshold of 3.5 mmol/l on Glow or other statistically low glucose level from the literature, or based on child or adult thresholds for damage, we have no evidence that treatment to achieve this outcome is beneficial. I also note from your Glow reference, 3 mmol/l is above the tenth centile until 72 hours, which seams a very conservative threshold to base your treatment threshold on. I am concerned about using Congenital Hyperinsulinism thresholds at such an early stage in infants who many will have a transient (self limiting-ref (C)) form of Hyperinsulinism. Is there even any evidence that aiming for 3.5 mmol/l or more reduces significant hypoglycaemia (eg <1.0 mmol/l) in the first week ? It is perfectly plausible it could do the opposite by feeding the insulin response.	Thank you for you comprehensive and referenced comments. We agree and the aim is not for well babies to be over-medicalised It is not possible to identify infants with significant hyperinsulinism until results of investigations are available. The higher operational threshold for those with suspected / confirmed hyperinsulinism (3.0 or 3.5mmol/L depending on age), should be used until babies are identified – this should be early on in life when investigations are performed according to practice point 21. Not that we can find. In the absence of evidence, we have aimed to align with advice from endocrinologists who will be advising about subsequent input

		No one is suggesting infants who have had GIR >8 mg/kg/day for several days-weeks and are perhaps being readied for home with glucose monitoring or on diazoxide should not be moved to this threshold predischarge or sooner if their GIR is sky high, but I would respectfully suggest this process is out with the scope of your guidance timeframe. Consider defining "suspected HI"-is this if the infants GIR is more than 8 ? So infants who are below this level can be defined as not currently reaching threshold or no longer likely to have HI and can be run at the lower sugar thresholds of 2 for the first 48 hours and 3 after 48 hours ? Many infants who end up with hypoglycaemia screens will be found to have a transiently high insulin levels, so any infant who has been screened could therefore reasonably be defined by clinicians as suspected HI even though there GIR comes down rapidly to normal. Consider wording this in a way that unless there is a high GIR then ongoing HI is unlikely and they should not labelled as suspected HI.	
		Your statements regarding practice point 25 in the different sections and references for this appear confusing. On page 16 you state: "*The recommended operational threshold should be 3.0mmol/l in neonates with suspected hyperinsulinism in the first 48 hours after birth[68] and 3.5mmol/l after 72 hours of age[69].*" From this I am left unsure what to do between 48-72 hours ?	This has been reworded
		On page 18 under practice points 22-24 (although I think you are talking about practice point 25) you state: "*If HH is suspected, diagnosis should be made promptly by confirming high plasma insulin levels and BG levels should be maintained >3.0mmol/l during the first 48 hours; increasing to an operational threshold of 3.5mmol/l from day 3[68].*" Day 3 will be confusing consider using hours.	Agree. This has been amended.
		Flow chart C states: "*Continue to monitor blood glucose until infant is on full enteral feeds and blood glucose values are >2.5mmol/l or 3.0mmol/l in cases of*	Agree. This has been amended.

		hyperinsulinism (after 48 hours increase to >3.5mmol/l for all babies) over several fast-feed cycles for at least 24 hours" This excludes suspected/confirmed part of the statement, and also suggests all infants will be moved to the 3.5 mmol/l threshold, consider clarifying. Your references (I can find no good evidence for your above statements from your references): 68: -The Diagnosis and Management of Hyperinsulinaemic Hypoglycaemia"quotes: "*It is paramount to diagnose HH as early as possible to avoid hypoglycaemic brain injury. Despite the difficulty in defining a cut-off concentration of blood glucose that suits all ages and conditions that present with hypoglycaemia, the level most consistently used worldwide to define hypoglycaemia for patients with HH is 3.5 mmol/L (63 mg/dL). This higher threshold of blood glucose concentration is recommended in view of the absence of ketones as an alternative source of energy for the brain in this group of patients. Patients with HH have glucose requirements >8 mg/kg/min (normal glucose requirements: 4-6 mg/kg/min) and this is also one of the diagnostic criteria for HH (1).*" This does not suggest a 48 hour cut off and is far from evidenced in the paper, which appears to be a review of hyperinsulinism by respected endocrinologists, and does not really appear relevant to the majority of infants with early transient low sugar levels that neonatologists see, which only a fraction will be referred onto endocrinologists. This is not a national review or guideline produced by any UK college or society. I am aware that there is a draft version of new national HI guidance being sent round to a select few neonatologists, that I am not privy too when trying to comment on your guidance. Let's hope they obtain a broad neonatal view of their guidance to balance the risks of over medicalisation with perceived risks of harm, in the absence of any clear evidence in this area. Reference (1) – from the paper above Practical management of hyperinsulinism in infancy, the only reference for the statements above.	Agree; amended

		Suggests a mixture of either 2.6-3 mmol/l (in text on pages F99/F102 and table 3), or above 3 mmol/l table 2. No specific time threshold is given such as 48-72 hours. Reference 69 Rennie and Roberton's textbook of neonatology, fifth edition. Publisher: Churchill Livingstone Elsevier, Edinburgh, 2012 There is no specific mention of 3.5 mmol/l or 48 or 72 hours ? Page 858 under Specific treatments, Hyperinsulinism the following is noted: Glucose delivery should be prescribed to maintain blood glucose levels above 3 mmol/l. This is in a section that suggests the infants not "self limiting" but severe cases in specialist centres. 3 mmol/l for hyperinsulinism is also mentioned in table 34.3 on page 859 several times. In summary: I and others are concerned that a move to aim for 3.5 mmol/l from 48 hours has increased the medicalisation of these infants with clear negative effects on their course leading it to be harder to wean them of IV fluids and stabilise on oral feeds, reducing breast feeding rates and increasing length of hospital stay. As it is not evidenced based we would suggest consider pushing this aim back to closer to a week of age in infants who fail a trial of weaning first and clearly still have a GIR > 8 mg/kg/min and or maybe infants with very high GIR >15. I would again respectfully suggest this process is out with the scope of your guidance timeframe. Refs A) Mukhopadhyay S, Wade KC, Dhudasia MB, Skerritt L, Chou JH, Dukhovny D, Puopolo KM. Clinical impact of neonatal hypoglycemia screening in the well-baby care. J Perinatol. 2020 Sep;40(9):1331-1338. doi: 10.1038/s41372-020-0641-1. Epub 2020 Mar 9. PMID: 32152490; PMCID: PMC7442584. B) What is hypoglycaemia? Part 1. | Neonatal Research	

		C) Rennie and Roberton's textbook of neonatology, fifth edition. Publisher: Churchill Livingstone Elsevier, Edinburgh, 2012	
Page 24		I would feel more than teaching mothers to hand express is needed and would not be supported by UNICEF breast feeding friendly indicative/BAPM optimisation early maternal breast milk toolkit, for what could be many days. Consider adding more breast milk expression support information or referencing these sources.	Outside remit
Page 27	Appendix 4	Also flow chart C, The use of mg/kg/min in the guidance in general leads to the use of glucose calculators, in practice as few people use your equations which appear confusing and do not supply a vital step to allow calculation of required high and low glucose volumes. Glucose calculators are defined by the MHRA as a medical device and should have their approval. Consider producing one and requesting MHRA approval. Continued use of non-approved glucose calculators must be seen as a clinical risk. Otherwise, you would need to supply and suggest the use of 4 equations and I am not sure this is something the majority of clinicians should or will use in practice. Regarding appendix 4, if the infant is on IV fluids already from flowchart C, or from flowchart B (although it doesn't suggest volumes) the infant will start on 10% glucose at maybe 60-100 ml/kg/day, from your table or equation (see below) I can work out the current GIR in mg/kg/min, but do I not then need the following equation to work out the new glucose concentration to be able to use this for the later equations ? Glucose % = 144 x new planned GIR (mg/kg/min) / Rate (ml/kg/day) I can then work out the new volumes of lower and higher sugar concentration sugar solutions to use.	Agree – many people utilize glucose calculators. Outside remit Amended

		I think in practice the need for 4 different equations and the possibility of error leads clinicians to use a calculator. Would a better format for your concentration of glucose equation be: GIR (mg/kg/min) = Rate (ml/Kg/day) x Glucose (%) / 144 Your current equation would allow the following to be done Rate/ (144 x glucose%) which I did and is wrong.	
Page 34-35	Flowcharts A, B and C	Flow chart A & B mention 48 hours, do not seam to cover 48-72 hour period Flowcharts A &B are very focused on management up to admission but do not cover much on weaning off iv fluids. Weaning off iv fluids in these infants in a timely safe process is so critical to avoid the over medicalisation of these infants it really feels like it should be critical to this guidance, especially as it now goes up to the 72 hour period. Consider adding this guidance. Also Flowcharts A and B really only go up to 24 hours, and have no information about weaning up on feed volumes, reducing feed interval or spacing this out again. Consider adding this guidance. More guidance around when and how to obtain good vascular access should also be considered. Consider adding more information to support maternal breast milk expression, continuing enteral feeds at a background level and specifically suggesting additional fluid increments should be given as some form of milk rather than as iv fluids once stability has been obtained. Or consider reducing the timescale for your guidance to 24 hours.	Title of flowchart amended. See Flowchart C. There is limited evidence available regarding weaning i.v fluids and detailed management of babies on neonatal units receiving i.v. fluids is outside the remit. Outside remit Agree; information leaflet amended

Page 20	First paragraph third paragraph under skin-to-skin	Typo “bloodglucose” “asoften” Typo “bloodtests” Typo ”andwarm” “makesure” “giveyour”	Thank you – there was a formatting issue following uploading
Page 21		Typo “ofhunger” “startto” “watchthe” Continue on to page 22	Thank you – there was a formatting issue following uploading

Zoe Salter, Specialist Midwife, Infant Feeding Team Lead, UNICEF Baby Friendly Initiative

Page number/ heading / general comments	Line number/ ‘general’ for comments	Comments Please insert each new comment in a new row.	
Pg 9	13.	We have a QI project using donor milk to support hypoglycaemic babies if mother is breastfeeding, this has been running for some years now with good results.	Thank you
Need for hats when skin to skin		It is my understanding through research, that as long as skin to skin is done with the mother who has given birth and the room is warm, blankets over baby appropriately etc then hats simply interfere with that babies reflexes and ability to latch to the breast, therefore potentially delaying feeding.	We recommend use of a hat as part of thermal care of newborns in hospital.
Use of formula is mothers milk not available		Skin to skin, when done correctly, can maintain a babies blood sugar whilst waiting for mothers milk to be available. In my clinical experience these babies don’t always need a ‘food’ to maintain healthy BG levels. By introducing formula early we are impacting on mothers milk supply, therefore negatively impacting her long term health and that of her baby.	Disagree

Pratik Shah and Ritika Kapoor, British Society for Paediatric Endocrinology and Diabetes (BSPED)

[Not sure if the comments below capture everything from BSPED, as I could not open the document Pratik sent. This summarises the email trail that accompanied it, however both Pratik and Ritika are members of the working group – Marcus.]

I feel a bit concerned by accepting a BG >2.0 on 2 occasions which then does not require any further testing – I would perhaps add further BG should be done if there is a deterioration in feeding or clinical concerns Response: this is stated inFfP

Page 18

The recommended operational threshold should be 3.0mmol/l in neonates with suspected hyperinsulinism in the first 48 hours after birth68 and 3.5mmol/l after 72 hours of age69. The operational threshold should be increased to at least 2.5mmol/l in infants with moderate-severehypoxic-ischaemic encephalopathy (for review see61), and it is possible that higher BGconcentration may confer benefit in this patient group71-73.

Not sure if the above has been misinterpreted, but I would suggest a threshold of < 3.0mmol/l after 48 hours for investigation, < 3.5 is too high and not practical , the UK consensus has agreed on < 3.0 to avoid over investigation and incorrect diagnosis of CHI. Response: These are treatment thresholds for babies with suspected / confirmed hyperinsulinism; investigations are triggered by >2 BG <2.0mmol/L.

It is reasonable to aim to keep BG > 3.5, but not use < 3.5 for investigations Response: Agree
The flow charts could be easier to read and also increasing glucose by 2mg/kg/min is not easy for everyone- need to be clearer

1- The threshold for investigations should align with either the international HI guidance (was submitted to ESPE for approval last summer but I can't seem to see it in print yet) and the UK group plans (which is not finalised yet).
2- Same for the investigations suggested. It would be good not to create confusion.
3- Ketone bodies vague and some may think it is bed side ketones.
4- I think it would be good for Guftar to comment although believe he may be on A this week and most of next week.
5- There is no description of the process of development or updating of these guidance. I would like to see a short paragraph of this in the document eg any lit review or how they came to the agreement.
6- There should also be a date to the finalized document and a review date.

Guftar Shaikh, Consultant in Paediatric Endocrinology & Honorary Clinical Associate Professor, Royal Hospital for Children, Glasgow

On behalf of UK CHI consensus group

Page number/ heading / general comments	Line number/ 'general' for comments	Comments Please insert each new comment in a new row.	
		Title states hypoglycaemia 72 hours, but text often mentions 48 hrs Executive summary: this is often read more avidly than the full text. There is no mention of a time scale between 2 reading of <2.0 mmol/L. The full text states <8 hours from birth, but it would be better to use a shorter time scale (if feeding 3 hourly, 3 hour time difference). Also need to state Blood glucose should be higher beyond 48 hours and should be investigated if still <3.0	FfP states babies should be fed with no greater than 3 hourly interval during this time period and 2 consecutive BG >2.0mmol/L are required This is included in several places
		Executive summary and practice points: only emphasis on blood gas analyser reading. Point of care (POC) testing devices are equally capable and require small blood volumes and therefore have a lower chance of failure. Inadvertent delay because of failed capillary blood testing can be minimized by rapid POC testing, minimizing the harm from hypoglycaemia	Thank you. Please see appendix
Page 7		Mentions high risk groups , should also include previous child with CHI//metabolic condition/hypoglycaemia- but unclear what blood glucose would be acceptable in the high risk groups Do not think a BG>2.0mmol/l is adequate in these high risk groups , esp infant of T1DM	We agree – and where possible this should be planned in advance of birth.
		Blood glucose of 2.0mmol/l – does seem low – need to make clear – blood glucose beyond 48/72 hour in normal term infants is >3.5mmol/l, and we recommend investigations if BG<3.0mmol/l in those >48/72 hours old and also if Blood glucose remain borderline bt 3.0-3.5 beyond 48 hours – needs to be assessed and discussed with appropriate specialist centre	We have emphasised the change in treatment threshold from 3.0mmol/L <48 hours of age and 3.5mmol/L from 48 hours in babies with suspected hyperinsulinism whilst awaiting input from specialists

		whilst we realise this document is for hypoglycaemia in first 48/72 hours – this will be the first document – midwives/neonatologists will refer to	
Flow charts		Having repeated low blood sugars needs further assessment/investigation If hypoglycaemic -according flow chart B- to have further blood glucose monitoring , so if 2 subsequent blood glucoses are >2.0mmol/l – no further monitoring required For example, initial blood glucose is 1.8mmol/l and then subsequent glucoses are 2.1 and 2.2- would you stop further glucose monitoring?? Suggest subsequent blood glucose levels should be higher>3.0, especially as infant is now older, or at least further glucose monitoring	Correct Yes
		Discharge to the community in at or <24 hours is too hasty and risks hypoglycaemia at home.	Discharge is after at least 24 hours in a baby who is feeding well
Pg 10		Investigations for hypoglycaemia (page 10): good that insulin is prioritized, but there is no addition of C-peptide	Agree; amended
Pg 11		The statement of 2 glucose <2.0 mmol/L in the 1st 48 hours is not time-sensitive. As the flowcharts discuss 3 hourly feeding intervals, a 3 hour interval should be specified in the very least. Hypoglycaemia in CHI is time critical, even in the first 72 hours. Newborns with CHI presenting in the 1st 72 hours often have severe and recurrent hypoglycaemia, therefore it is essential that the time window is specified (even if asymptomatic). Point 19- would suggest using 0.5mg glucagon If CHI is suspected as per recent and emerging CHI guidelines (in submission as a manuscript, under the CHI- special interest group, British Society for Paediatric Endocrinology and Diabetes), glucose treatment threshold should be increased to 3.5 mmol/L. This ensures a lower risk of hypoglycaemia induced brain injury from CHI	Disagree; likely to be confusing.

		(combination of severe hypoglycaemia and low ketones). It is confusing to have 2 thresholds 3.0 and 3.5 mmol/L at an arbitrary cut-off time of 48 hours. This runs the risk of misinterpretation. Further, as CHI is relatively rare, a higher threshold does not risk escalation of treatment in a significant additional group of newborn babies but is a safer option. If CHI is suspected- should aim BG> 3.5 mmol/l regardless of 48hrs or not. If a baby is suspected to have CHI, the baby should be reviewed by the neonatal team and moved to NICU. This is not clear in the framework. – also infant to be discussed with local CHI centre. point 24: glucose requirement >8 mg/kg/min is used a marker for predicting hyperinsulinism in the post-natal ward. This is not practical as many mothers breast feed and midwives do not typically measure glucose infusion rate from formula feeds. Further, standard infant formula at 90 ml/kg/day only provides 4.3 mg/kg/min. It is not conceivable that newborn babies feed at 180 ml/kg/day in the 1st 72 hours. Therefore, the glucose requirement applies more to those on intravenous fluids (in NICU) than to those fed orally	Disagree; clinicians caring for newborn babies are used to changes / differences with increasing postnatal age / gestation and we do not agree that this is confusing. Location of babies depends on level of medical intervention required. Disagree that it is necessary to advise discussion of baby with suspected CHI with CHI team. The glucose infusion rate applies to iv glucose and would not be calculated by midwives but neonatal doctors prescribing iv fluids
Pg 15-16		Measuring urinary ketones in newborns <48 hours old is not practical and not of much use (as they do not generate ketones) and should be removed. Blood ketones by POC may be a better option Threshold for intervention (page 15-16) has no mention of CHI, as thresholds for treatment are different in CHI in contrast to non-CHI hypoglycaemia. There is no acknowledgement of a higher risk of neurodevelopmental defects in CHI because of the severity of hypoglycaemia and the absence of neuroprotective ketones	Amended
Pg 18		Threshold for investigation not clear why use a lower threshold for HIE (2.5mmol/l) but not CHI Threshold for investigation beyond 72hrs of < 3.5 mmol/l is too high and will result in over-investigation , unless there are other risk factors , eg increased GIR	These are treatment thresholds not thresholds for investigation
Pg 21		Note – insulin levels will not be available so soon (within 48 hours)	Disagree

		If CHI is suspected within 48 hours – BG levels should be maintained >3.5 mol/l , ideally >4.0- through IV dextrose and/or glucagon and discussed with local CH centre	
		The term Hyperinsulinaemic Hypoglycaemia (HH) is correct but is now rarely used. The two most common terms are Congenital Hyperinsulinism (CHI) and Hyperinsuslinism (HI), the former being preferred in the UK and Europe and the latter more commonly used in the US. Syndromes (page 21): list has no introductory text. It is not helpful to state "+ others". Prader Willi syndrome is not typically associated with CHI and should be removed. The term "ambiguous genitalia" is insensitive and should be replaced by abnormal appearing genitalia.	Amended Amended but disagree about use of abnormal appearing genitalia which could risks inclusion of babies with minor abnormalities.
		Appendix 4 should also have the dextrose bolus dose as in Flowchart C.	Disagree
Pg 30		The formula for glucose mg/kg/min should have brackets as [Rate (ml/kg/day) / 144] x glucose% = mg/kg/min	Amended
		Familial glucocorticoid deficiency (FGD) is an extremely rare form of hypoglycaemia (even for endocrinologists) and is rarely associated with neonatal pigmentation. Neonatal pigmentation may be misleading and cause unnecessary anxiety in those in communities from a diverse ethnic background. Congenital Adrenal Hyperplasia (CAH) is commoner and in the absence of a national screening programme, may be missed. However, as neonatal pigmentation is misleading, it would not be appropriate CAH as a cause for neonatal hypoglycaemia simply on ground of excess pigmentation. Of course, CAH may be suspected in those with abnormal genitalia, but this rule does not apply for males born with 21 hydroxylase CAH.	Amended
		Reference 68 is not a valid reference to justify supporting a lower threshold (3.0 mmol/L) in the 1st 48 hours.	Amended (supports 3.5mmol/L)
		Has the guideline been discussed with Inherited Metabolic Diseases	Thank you

Annette Thomas, Chair National Point of Care Strategy Board, Consultant Clinical Scientist, National Clinical Lead for Point of Care Testing

Thank you for the opportunity to comment on the recent update of the guidelines for the Identification and Management of Neonatal Hypoglycaemia in the Full term infant. The attached document National POCT SB Response to BAPM 2023 guidelines reflects the views of the National Point of Care testing Strategy Board in Wales. Our comments relate specifically to the POCT glucose testing section in the guidelines and the evidence supporting the performance of certain POCT glucose devices. I also attach a list of published and unpublished (local evaluation) data that we reviewed as part of the response to the document for your consideration.

See separate email: "Consultation_Responses_Hypoglycaemia_Annette_Thomas" which contains a number of documents

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