

ONLINE-ONLY SUPPLEMENTS

eFigure 1 CGM device

eFigure 2 Prisma flow chart

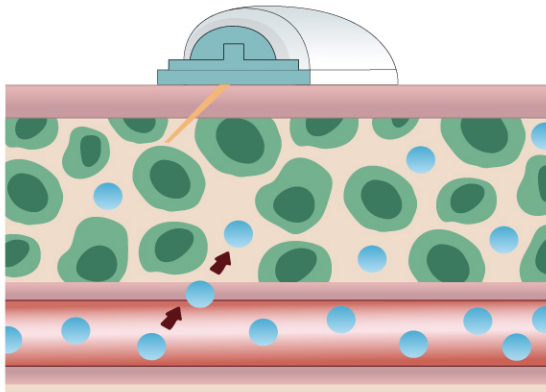
eTable 1 (a-e) Data extraction: 3x3 contingency tables showing the paired glucose values between the reference standard and the index test. The threshold used for hypoglycaemia was <2.6 mmol/L and for hyperglycaemia >10 mmol/L.

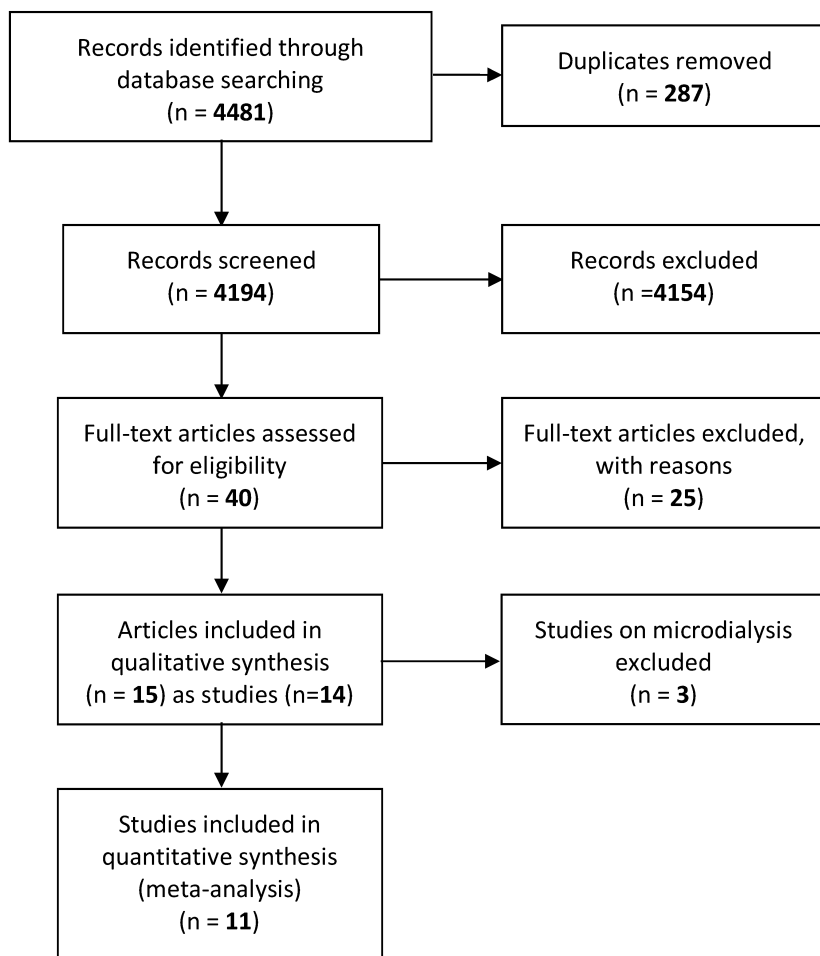
eTable 2 Characteristics of excluded studies

eTable 3: Included studies characteristics

Search strategy

Microdialysis articles

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eTable 1 Characteristics of excluded studies

Study ID	Reason for exclusion
Alonso et al. 2014 ⁵⁹	Editorial
Hay Jr et al. 2010 ⁶⁰	Editorial
Hernandez et al. 2019 ⁶¹	Editorial
Beardsall et al. 2011	Duplicate of Beardsall et al. 2013 ³⁴
Beardsall et al. 2012	Duplicate of Beardsall et al. 2013 ³⁴
Bondy et al. 2018	Duplicate of Nally et al. 2018 ³⁸
Barrio Castellanos et al. 2010 ⁶²	Duplicate of Harris et al. 2010 ³² in Spanish
Thomson et al. 2018b	Duplicate of Thomson et al. ⁴⁶
Harris DL et al, 2010 ³²	Patients included are both term and preterm, stratified data not provided
Conrad et al. 2004 ⁶³	Patient age ranges from 6 months to 17 years
Stewart ZA et al. 2019 ³¹	Patients included are both term and preterm, stratified data not provided
Wackernagel D et al. 2016 ³³	One preterm patient, no hyper- hypoglycaemic events
McGlacken-Byrne et al. 2019 ⁶⁴	Patients included are term infants
Sanchez de Leon et al. 2012	Patients included are term infants
Mizumoto et al. 2012	Abstract published in journal
Mola Riehle et al. 2012	Abstract published in journal
Wackernagel et al. 2012	Abstract published in journal
Signal et al. 2011	Abstract published in journal
Nakamura et al. 2016 ⁶⁵	Case report
Saha et al. 2018 ⁶⁶	Case report
Signal et al. 2012b	Poster for Signal et al. 2012 ⁶⁷
Signal et al. 2012 ⁶⁷	They study the effect of calibrating CGM devices
Javid et al. 2005 ⁶⁸	They study Extracorporeal Glucose Monitoring System (EGMS), not CGM devices
Jagla et al. 2018 ⁸	They do not compare the CGM with any other glucose testing modality
Tsao et al. 2017 ⁶⁹	They study a type of intermittent glucose monitoring

eTable 2 (a-e) Data extraction: 3x3 contingency tables showing the paired glucose values between the reference standard and the index test. The threshold used for hypoglycaemia was <2.6mmol/L and for hyperglycaemia >10mmol/L.

(a) Pertierra-Cortada ⁴⁴		Reference standard (PoC)		
Index test (CGM)		Hypoglycemic	Normoglycemic	Hyperglycemic
	Hypoglycemic	0	3	0
	Normoglycemic	2	402	0
	Hyperglycemic	0	0	0

(b) Iglesias-Platas ⁴²		Reference standard (PoC)		
Index test (CGM)		Hypoglycemic	Normoglycemic	Hyperglycemic
	Hypoglycemic	1	2	0
	Normoglycemic	9	871	16
	Hyperglycemic	0	10	115

(c) Tomotaki ³⁵		Reference standard (PoC)		
Index test (CGM)		Hypoglycemic	Normoglycemic	Hyperglycemic
	Hypoglycemic	1	0	0
	Normoglycemic	3	260	0
	Hyperglycemic	0	3	2

(d) Nally ³⁸		Reference standard (PoC)		
Index test (CGM)		Hypoglycemic	Normoglycemic	Hyperglycemic
	Hypoglycemic	5	5	0
	Normoglycemic	0	49	0
	Hyperglycemic	0	0	0

(e) Tabery ³⁹		Reference standard (PoC)		
Index test (CGM)		Hypoglycemic	Normoglycemic	Hyperglycemic
	Hypoglycemic	2	6	0
	Normoglycemic	0	72	0
	Hyperglycemic	0	0	0

eTable 3: Included studies characteristics

	Reference standard	Adverse effect	Inclusion/exclusion criteria
Beardsall 2005 ¹³	PoC: The Elite (Bayer, Munich, Germany) and Medisense (Abbott, Abbott Park, Illinois, USA) near patient glucose monitors.	In one baby of 23 weeks gestation, in whom 50/50 paraffin had been used because of very poor skin condition, the sensor fell out on two occasions and was therefore not replaced. In another baby (24 weeks gestation) a small area of superficial skin loss was noted 24 hours after sensor removal, but this healed well.	Inclusion: infants requiring intensive care and born <1500 g
Beardsall 2013 ³⁴	PoC: Leuven, Genk and Leeds, Radiometer (Radiometer Medical ApS, Denmark); Cambridge and Barcelona, Bayer Elite XL (Bayer, Germany); Luton, Medisense (Abbott, Illinois, USA), Amsterdam, HemoCue Glucose Analyser (HemoCue AB); and Edinburgh, Yellow Springs Instrument (YSI (UK), Hampshire, England).	Well tolerated There were 4 controls, where CGMS data were not available, due to a combination of early death, or sensor failure.	Exclusion: maternal diabetes and major fetal congenital abnormalities
Iglesias-Platas 2009 ⁴²	PoC: Ascensia Elite XL (Bayer Vital, Leverkusen, Germany) bedside monitor	Well tolerated	Exclusion: babies born to diabetic mothers (both gestational and pre-existing diabetes); babies with any major congenital anomaly.
Nally 2019 ³⁸	Precision Xceed Pro Glucose Monitoring System (Abbott Laboratories, IL). □□ Calibration - Contour Next Glucometer (Ascensia Diabetes Care, Parsippany, NJ).	One infant had mild bleeding upon sensor placement that necessitated removal because of a sensor failure error. One infant retained the sensor wire upon removal of the sensor, which is a very rare, but known risk. This infant did not require any medical intervention related to the retained sensor wire. Early in the study, two additional sensors failed the initial warm-up period after insertion and were removed. This was avoided in future participants by repeating the sensor warm-up period and not removing the sensor. Three infants were unable to complete the study because of sensor failures after placement.	Inclusion: infants born to mothers with a diagnosis of diabetes during pregnancy, including type A1 (diet-controlled gestational diabetes), type A2 (medication-controlled gestational diabetes), type 1 diabetes, or type 2 diabetes. Exclusion: birth before 34 weeks of gestation, weight <2000 g, or if the infant received a medication known to affect sensor values (i.e., acetaminophen).
Perri 2018 ⁴³	PoC: Medtronic Stat Strip Xpress	Well tolerated	Inclusion: VLBW and central line positioned to administer parenteral nutrition. Exclusion: newborns with major congenital abnormalities at birth or with skin diseases
Pertierra-Cortada 2014 ⁴⁴	PoC Ascensia Elite XL (Bayer Vital, Leverkusen, Germany)	Well tolerated	Inclusion: VPT infants (= <32 weeks) admitted to NICU and approaching discharge, which usually takes place after 35 weeks PMA and near 2 kg of weight. Exclusion: infants born to mothers with diabetes and with congenital anomalies or complications of prematurity requiring fluid restriction or continuous feedings
Saw 2017 ⁴⁵	A-line	Well tolerated	Exclusion: premature infants born with any major congenital malformations, including chromosome abnormally, confirmed or suspected sepsis or

			pneumonia, in a terminal state on admission, umbilical anomaly, skin infection, or conditions that prevented sensor attachment
Tabery 2018 ³⁹	PoC/lab test (blood gas analyzer (ABL800; Radiometer Medical ApS; Brønshøj; Denmark) or by a blood glucose meter (Stat Strip; Nova Biomedical Corporation, Waltham, MA; USA)	Well tolerated	Inclusion: infants born to diabetic mothers, birth 35th week of gestation Exclusion: congenital developmental defects or perinatal asphyxia.
Thomson 2019 ⁴⁶	PoC: combination of arterial, venous or capillary samples and tested on the blood gas analyser (Cobas b221; Roche Diagnostics, UK), and the Nova StatStrip (Nova Biomedical, Massachusetts, USA)	Well tolerated	Inclusion: birth weight <1200g, age <48hours and written informed parental consent Exclusion: major congenital malformation, any underlying metabolic disorder or if mothers had diabetes mellitus.
Tiberi 2016 ⁴⁷	PoC (no information about the device)	Well tolerated	Inclusion: preterm infants at increased risk for neonatal dysglycemia for intrauterine growth-restricted (IUGR) infants, small for gestational age infants (SGA), very low birth weight (VLBW) infants, extremely low birth weight (ELBW) infants, infants of diabetic mothers, maternal treatment with beta-blockers, tocolytics, oral hypoglycemic therapy, large for gestational age (LGA) infants, asphyxiated infants, septic infants, polycythaemic infants, infants with feeding difficulties. Exclusion: major congenital abnormalities at birth or with skin diseases.
Tomotaki 2019 ³⁵	PoC: StatStrip Xpress900 (Nova Biomedical, Waltham, MA, USA).	Well tolerated	Inclusion: at least one of the following: (i) symptomatic hypoglycemia; (ii) difficulty stopping i.v. continuous glucose infusion because of hypoglycemia; and (iii) difficulty stopping infusion of enteral feeding by a gastric tube because of hypoglycemia. Exclusion: serious congenital abnormality, skin condition that contraindicated insertion of the sensor, or absence of parental agreement

Search strategy:

PubMed: (("Blood Glucose"[Mesh] AND "Monitoring, Physiologic"[Mesh]) OR continuous glucose monitor* OR CGM[Title/Abstract] OR "glucose control") AND (infant, newborn[MeSH] OR newborn*[TIAB] OR "new born"[TIAB] OR "new borns"[TIAB] OR "newlyborn"[TIAB] OR baby*[TIAB] OR babies*[TIAB] OR premature[TIAB] OR prematurity[TIAB] OR preterm[TIAB] OR "pre term"[TIAB] OR "low birth weight";[TIAB] OR ";low birthweight";[TIAB] OR VLBW[TIAB] OR LBW[TIAB] OR infan*[TIAB] OR pediatric[Title] OR neonat*[TIAB])

Embase: (('blood glucose monitoring'/exp) OR ('monitoring'/exp AND 'glucose blood level'/exp) OR ('continuous glucose monitor*' OR cgm:ti,ab OR (glucose NEAR/3 control*) OR (glucose NEAR/3 monitor*))) AND (('prematurity'/exp OR 'infant'/exp) OR (newborn*:ti,ab OR 'new born':ti,ab OR 'new borns':ti,ab OR 'newly born':ti,ab OR baby*:ti,ab OR babies:ti,ab OR premature:ti,ab OR prematurity:ti,ab OR preterm:ti,ab OR 'pre term':ti,ab OR 'low birth weight':ti,ab OR 'low birthweight':ti,ab OR vlbw:ti,ab OR lbw:ti,ab OR infant:ti,ab OR infants:ti,ab OR infantile:ti,ab OR infancy:ti,ab OR neonat*:ti,ab))

CINAHL: (MH "Blood Glucose Monitoring+") OR (MH "Blood Glucose") AND (MH "Monitoring, Physiologic+") OR (continuous glucose monitor* OR TI CGM OR AB CGM) OR (glucose N3 monitor* OR glucose N3 control*) AND ((infant or infants or infantile or infancy or newborn* or "new born" or "new borns" or "newlyborn" or neonat* or baby* or babies or premature or prematures or prematurity or preterm or preterms or "pre term" or premies or "low birth weight" or "low birthweight" or VLBW or LBW))

Cochrane Library: (infant or infants or infantile or infancy or newborn* or 'new born' or 'new borns' or 'newly born' or neonat* or baby* or babies or premature or prematures or prematurity or preterm or preterms or 'pre term' or premies or 'low birth weight' or 'low birthweight' or VLBW or LBW or ELBW or NICU) AND (([Blood Glucose] AND [Monitoring, Physiologic]) OR (continuous glucose monitor* OR cgm OR 'glucose control'))

Microdialysis articles

Three studies from the 90's and early 2000's were about microdialysis used on infants^{36,37,40,41}, a technique where a catheter was introduced in the subcutaneous skin to monitor the diffusion of small molecules from the blood to the extracellular space including, amongst others, glucose, urea and lactate. At the time this technique was new and the authors of these articles studied the device on patients at NICUs because they were keen to find an alternative method for monitoring glucose without drawing blood. Baumeister et al.⁴⁰ report that microdialysis might be used for glucose monitoring in infants during intensive care, but that further research is warranted. De Boer et al.^{36,37} report that microdialysis might be used to monitor glucose in infants, and that the results are more accurate if the microdialysis device is calibrated. Hildingsson et al.⁴¹ report a great similarity between serum glucose and the glucose level in the interstitial fluid, and that microdialysis might be implemented as a method for glucose monitoring in this population in the future. These studies fit our inclusion criteria and we were therefore unable to exclude them, however they are irrelevant for the clinical context of the present review and are therefore not included in the quantitative synthesis.

Risk of bias in included studies

Three of the eleven included studies had a high risk of bias on patient selection^{42,44,46}, mainly because they excluded infants born to diabetic mothers and it was unclear why they choose to exclude a population of infants that are at risk of altered blood glucose. However, this exclusion was deemed to have a low impact on the applicability, because these infants constituted only a small portion of the total population of preterm infants. One study⁴⁵ had an unclear risk of bias on patient selection and considerable concern for applicability in the same domain, because they did not accurately report how the patients were recruited.

Risk of bias and applicability concerns were low with regard to the index tests used in the included studies.

Four studies out of eleven studies had high risk of bias regarding the reference standard^{35,38,43,45}, because they used alarms on their CGM devices when the reading was above or below the pre-decided thresholds. In this case an additional PoC test would be performed. This leads to tests being more likely to be performed when the glucose level is pathological, and therefore constitutes a risk of partial verification bias.

Another concern in this domain was the level of accuracy of the reference standard devices. In fact, even if commonly used PoC devices may have a deviation from the true value of 10% to 30%^{48,49}, we assumed those method of measurement as a reference standard, as they are the most frequently used in clinical practice in the NICU as compared to laboratory enzymatic methods due to being more readily available and less invasive than taking blood samples which must be sent to a laboratory. All but one study⁴⁵ used PoC glucometers as their reference standard. Considering that to determine the accuracy of a test by comparing it to an inaccurate reference could introduce a misclassification bias, we decided to define not at risk those PoC devices which satisfied the minimum accuracy requirements stated by the International Organization for Standardization (ISO)⁵⁰. Seven studies^{13,34,35,38,42-44} had high risk of bias⁵¹. One study⁴⁷ had unclear risk of bias because they did not report which brand of PoC device they used. The study of Saw et al.⁴⁵ used a laboratory enzymatic method as a reference standard, so it was considered at high risk of bias in this domain, because of the difference in accuracy that this method could have in respect of PoC devices^{48,49}.

There was a high risk of bias regarding flow and timing in three studies^{13,34,39} of the eleven included studies, as they used several different brands of PoC devices as their reference standard, each with a different level of accuracy¹⁶.