Management of type 1 diabetes in pregnancy: update on lifestyle, pharmacological treatment, and novel technologies for achieving glycaemic targets

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Glucose concentrations within target, appropriate gestational weight gain, adequate lifestyle, and, if necessary, antihypertensive treatment and low-dose aspirin reduces the risk of pre-eclampsia, preterm delivery, and other adverse pregnancy and neonatal outcomes in pregnancies complicated by type 1 diabetes. Despite the increasing use of diabetes technology (ie, continuous glucose monitoring and insulin pumps), the target of more than 70% time in range in pregnancy (TIRp 3·5–7·8 mmol/L) is often reached only in the final weeks of pregnancy, which is too late for beneficial effects on pregnancy outcomes. Hybrid closed-loop (HCL) insulin delivery systems are emerging as promising treatment options in pregnancy. In this Review, we discuss the latest evidence on pre-pregnancy care, management of diabetes-related complications, lifestyle recommendations, gestational weight gain, antihypertensive treatment, aspirin prophylaxis, and the use of novel technologies for achieving and maintaining glycaemic targets during pregnancy in women with type 1 diabetes. In addition, the importance of effective clinical and psychosocial support for pregnant women with type 1 diabetes is also highlighted. We also discuss the contemporary studies examining HCL systems in type 1 diabetes during pregnancies.

Introduction

Pregnancy in women with type 1 diabetes is associated with an increased risk of pregnancy complications, including congenital malformations, pre-eclampsia, preterm delivery, and perinatal mortality (appendix p 3). In addition, approximately 50% of infants born to mothers with type 1 diabetes are large for gestational age (LGA).[1–3] LGA can lead to problems during labour, including shoulder dystocia, which can result in neonatal birth trauma and has been associated with a long-term risk for type 2 diabetes in the offspring.[4] Several population-based cohort studies have shown that, despite new technologies for type 1 diabetes, birth outcomes have barely improved over time.[1,5,6] Although target glycaemia around the time of conception (HbA_{1c} should be <7·0% [53 mmol/mol] and preferably <6·5% [48 mmol/mol] at preconception) is essential for reducing the risk of congenital malformations and miscarriage, achieving and maintaining this target throughout pregnancy is needed to prevent other pregnancy complications.[7] However, maintaining this target is difficult due to several metabolic changes occurring during pregnancy in women with type 1 diabetes, such as the increased risk of hypoglycaemia in early pregnancy,[8,9] increased insulin resistance from approximately 16 weeks' gestation, and delayed insulin absorption from approximately 20 weeks' gestation (appendix p 4).[10]

The American Diabetes Association (ADA) recommends that HbA_{1c} should be less than 6·5% (48 mmol/mol) in early pregnancy and less than 6·0% (42 mmol/mol) in the second and third trimesters.[11] However, nationwide data from the UK has shown that, with current care options, less than 50% of women with type 1 diabetes have glycaemia within this target range during pregnancy.[1,12] Despite the increasing use of continuous glucose monitoring (CGM) and insulin pumps, pregnant women with type 1 diabetes continue to spend on average 8 hours per day above target glucose concentrations.[13,14] The 2019 Advanced Technologies and Treatments for Diabetes (ATTD) consensus on CGM targets included the aims that a CGM time in range in pregnancy (TIRp) of 3·5–7·8 mmol/L (63–140 mg/dL) should be achieved more than 70% of the time and time below range in pregnancy (TBRp) of less than 3·5 mmol/L (63 mg/dL) less than 4% of the time.[15] A Swedish cohort study showed that mothers of LGA infants had lower TIRp during the second (52% *vs* 58%) and third trimesters (58% *vs* 62%) than mothers of non-LGA infants, and a 5–6% lower TIRp was associated with a higher risk of neonatal adverse outcomes (eg, macrosomia, shoulder dystocia, hypoglycaemia, or neonatal intensive care unit [NICU] admissions).[14,16] Studies have shown that pregnant women with type 1 diabetes typically have TIRp of approximately 60%.[13,14,17,18] The target of more than 70% TIRp is often only reached in the final weeks of pregnancy, which is too late for optimal perinatal outcomes.

Hybrid closed-loop (HCL) systems that provide automated, glucose-responsive, basal insulin delivery with manual, self-administered, premeal insulin doses are emerging as promising treatment options in the management of type 1 diabetes in pregnancy.[19–23] However, most HCL systems are currently not approved for use in pregnancy and the gestational changes in insulin requirements could alter the effectiveness and safety of HCL systems that use algorithms derived from non-pregnant populations.

Reducing intake of carbohydrates with high glycaemic index and limiting gestational weight gain are also important to optimise antenatal glycaemia and to reduce

the risk for pregnancy complications.[24] In addition, pharmacological treatment with antihypertensive medications and low-dose aspirin might be needed to reduce the risk for pre-eclampsia and preterm delivery.[3,25] Therefore, a multitargeted approach that focuses on more than glycaemic management is needed (figure 1). In this Review we discuss the latest evidence on pre-pregnancy care, lifestyle recommendations, pharmacological treatment, management of diabetes-related complications, and novel technologies for achieving and maintaining glycaemic targets in pregnancies of women with type 1 diabetes. Attention should also be paid to the psychosocial effect of this multitargeted approach in pregnant women with type 1 diabetes. We also discuss the contemporary studies evaluating HCL systems in pregnancy of women with type 1 diabetes.

Pre-pregnancy care

Pre-pregnancy care programmes for women with type 1 diabetes are associated with increased intake of folic acid preconception, fewer women smoking, decreased consumption of potentially teratogenic medication at conception, and a lower HbA_{1c} throughout pregnancy compared with women not involved in these programmes.[26,27] Moreover, attendance at pre-pregnancy care programmes has shown to reduce or prevent several pregnancy complications, such as congenital malformations.[26,27] Improving pre-existing skills of glycaemic self-management is also important to minimise the risk of hypoglycaemia and hyperglycaemia in pregnancy. Besides achieving and maintaining glucose concentrations within target, gaining dietary advice by a specialist dietitian trained in type 1 diabetes to count carbohydrates and manage weight before pregnancy is recommended by health-care professionals. Despite pre-pregnancy care programmes being clinically effective and cost-saving, less than 40% of women with type 1 diabetes receive formal pre-pregnancy care.[27] Barriers for women with type 1 diabetes in attending pre-pregnancy care can include insufficient awareness, unclear communication from health-care providers, and logistical problems, such as difficulty in getting time off work and childcare.[27] Insufficient pre-pregnancy care can also be because of factors relating to the clinician, which might include the physician's insufficient knowledge about the importance of pre-pregnancy care, time constraints during appointments, and discomfort at discussing pregnancy and contraception.[27]

Management of diabetes-related complications

A history of severe hypoglycaemia within the past year, impaired hypoglycaemia awareness, longer diabetes duration, and HbA_{1c} maximum 6·5% (48 mmol/mol) in the first trimester can all increase the risk for severe hypoglycaemia in pregnancy.[9] Increased use of insulin analogues, insulin pump therapy, and CGM has reduced the incidence of severe hypoglycaemia alongside a reduction of insulin dose by 10–20% at 8–16 weeks' gestation and limiting supplementary insulin between meals.[28]

Diabetic ketoacidosis occurs in 0·5–10% of pregnancies with type 1 diabetes, and has a high risk for maternal-fetal morbidity and fetal loss (10–35%).[29] The altered metabolic environment of pregnancy means that diabetic ketoacidosis can develop more rapidly at less severe hyperglycaemia than in non-pregnant women and even during normoglycaemia (appendix p 4). Prenatal counselling of women with type 1 diabetes should therefore include and reinforce education on the prevention of diabetic ketoacidosis and associated symptoms.

Despite the aim to maintain glycaemic target ranges in women with type 1 diabetes during pregnancy, the progression of diabetic retinopathy remains higher than in non-pregnant adults with diabetes, with a pooled progression rate per 100 pregnancies for new diabetic retinopathy of 15 and worsened non-proliferative diabetic retinopathy of 31.[30] A 2021 study showed that elevated HbA_{1c} and a duration of diabetes of at least 10 years were risk factors for diabetic retinopathy progression and in women with pre-pregnancy diabetic retinopathy, treatment with an insulin pump decreased the risk for the progression of diabetic retinopathy.[31] Due to the increased risk for progression during pregnancy, screening for diabetic retinopathy in each trimester is suggested.[11,32] However, this can probably be safely reduced for women without diabetic retinopathy in early pregnancy and HbA_{1c} less than 7·0% (53 mmol/L), as these women are unlikely to develop sight-threatening diabetic retinopathy.[32]

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See Online for appendix

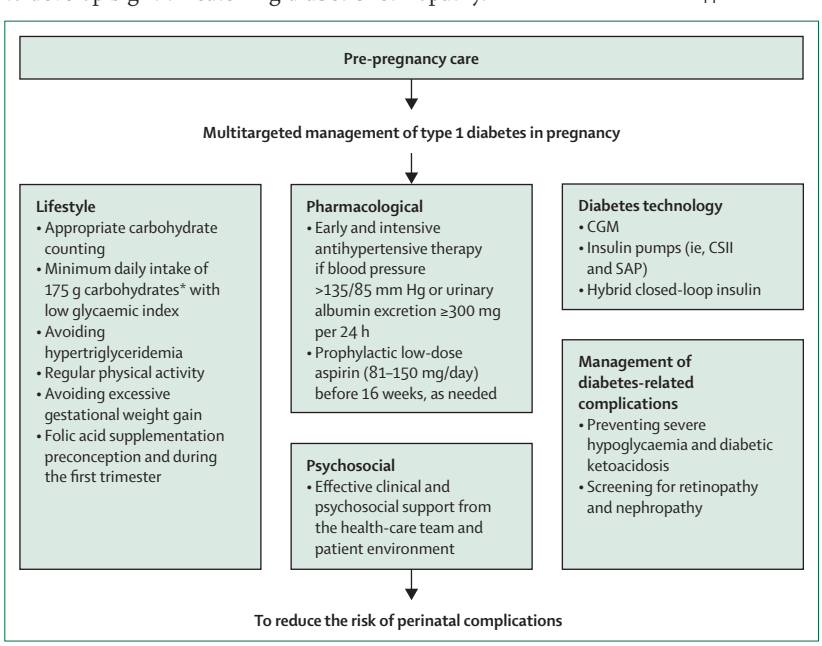

Figure 1: **Multitargeted management of pregnancies in women with type 1 diabetes, including pre-pregnancy care, lifestyle, pharmacological, psychosocial, and technology approaches, to reduce the risk for perinatal complications**

CGM=continuous glucose monitoring. CSII=continuous subcutaneous insulin infusion. SAP=sensor-augmented pump. *The recommended minimum intake of carbohydrates in pregnancy is uncertain because of limited evidence.

Pre-eclampsia and early preterm delivery (ie, <34 weeks) can occur in up to 60% of pregnancies in women with type 1 diabetes with nephropathy.[33] Nephropathy can also progress during pregnancy, therefore screening for proteinuria in each trimester is recommended (figure 1).[11,34]

Lifestyle recommendations

Dietary recommendations

In adults with type 1 diabetes, carbohydrate counting has been shown to reduce HbA_{1c} concentrations with reduced hypoglycaemia.[35] Carbohydrate quantity is also positively associated with HbA_{1c} in pregnancy in women with type 1 diabetes, suggesting that carbohydrate counting might also be important to facilitate glycaemic management in pregnancy.[36,37] Appropriate carbohydrate counting is also needed with HCL systems to provide an appropriate bolus to limit postprandial hyperglycaemia.

As the quantity of carbohydrate intake is the main dietary factor affecting postprandial glucose concentrations, a lowered proportion of carbohydrate intake (ie, 40% of total energy intake) during pregnancy has been suggested for women with type 1 diabetes.[38] In addition, the intake of carbohydrates with low glycaemic index (eg, bread, whole grain, and high-fibre fruit) is preferred because these products have a high content of fibres, which is shown to be inversely associated with insulin requirements in people with type 1 diabetes and has positive effects on postprandial glucose concentrations.[39] The amount of carbohydrate intake in pregnancy considered sufficient to prevent ketone concentrations is unknown. The National Academy of Medicine (NAM, previously known as the Institute of Medicine) guidelines recommend a minimum intake of 175 g of carbohydrates daily in pregnancy irrespective of BMI to promote typical fetal brain development and to limit the risk of ketone formation, which might be associated with a reduced childhood intelligence quotient.[40,41] This amount of carbohydrate can be obtained by consuming 20 g at breakfast, 50 g at lunch, 50 g at dinner, and three snacks of 10–20 g during the day. To avoid hyperglycaemia after breakfast because of increased insulin resistance in the morning, a low-carbohydrate breakfast has been suggested.[38]

In addition to hyperglycaemia, pre-pregnancy obesity and maternal lipid concentrations also have an important role in fetal overgrowth and its associated complications.[42] The proportion of people with obesity and type 1 diabetes is increasing.[43] Several studies have shown that elevated triglycerides in the first and third trimester and low HDL-cholesterol throughout pregnancy are predictive of LGA infants independent of chronic glycaemia in type 1 diabetes.[44,45] Type 1 diabetes has also been shown to lead to an augmented placental transfer of lipids, especially free fatty acids.[46] Losing weight before pregnancy to achieve a BMI of less than 25 kg/m², minimising gestational weight gain according to the NAM guidelines, lowering maternal triglyceride concentrations by a low-fat diet with reduced intake of saturated fat, and increasing fibre intake might lead to less excessive fetal growth and lower rates of pre-eclampsia.[42] However, to the best of our knowledge, data from randomised controlled trials specifically targeting the management of maternal lipids in pregnant women with type 1 diabetes are absent.

Despite the importance of an appropriate diet in pregnancy, diets of pregnant women with type 1 diabetes are often high in fat, low in fibre, and almost half of the daily carbohydrate intake derived from high glycaemic index sources.[47] To optimise maternal nutrition, counselling by a dietitian familiar with the management of type 1 diabetes in pregnancy should be offered to all pregnant women with type 1 diabetes.

To reduce the risk for congenital malformations, folic acid supplementation is recommended for all women at preconception and during the first trimester of pregnancy.[11] There is no consensus on the dose of folic acid and recommended doses range from 400 µg/day to 5 mg/day.[48] Although there are conflicting data on vitamin D supplementation, ensuring vitamin D is also maintained within the reference range during pregnancy is important.[49]

Physical activity

Exercise of low-to-moderate intensity in women with gestational diabetes has been shown to be safe and improve blood glucose. Therefore, most guidelines recommend that pregnant women with type 1 diabetes, especially if glycaemia is within target, should also engage in regular physical activity (eg, 150 min per week of moderate-intensity physical activity).[11,50,51] However, there are few studies that evaluated physical activity in pregnant women with type 1 diabetes.[50,52] The only randomised controlled trial on exercise—20 min of postprandial walking three times per week, starting in the late first trimester—in pregnant women with type 1 diabetes was published in 1987 and observed lower average glucose concentrations without increase in hypoglycaemia in the exercise group compared with the non-exercise group. Additionally, there were fewer caesarean sections and lower rates of neonatal hypoglycaemia and macrosomia in the exercise group compared with the non-exercise group.[52]

Gestational weight gain

The NAM recommends optimal targets for gestational weight gain based on pre-pregnancy BMI in women without type 1 diabetes: 11·5–16·0 kg for women with normal weight, 7·0–11·5 kg for women with overweight, and 5·0–9·0 kg for women with obesity.[40] Avoiding excessive gestational weight gain in women with type 1 diabetes is important as high gestational weight gain is associated with hypertensive disorders of pregnancy and increased offspring birthweight independent of glycaemic control and pre-pregnancy BMI.[24] Moreover, exceeding

the NAM guidelines for gestational weight gain in women with type 1 diabetes might also be associated with an increased long-term risk (odds ratio [OR] 7·50) for offspring to have overweight and obesity at adolescence.[53] For women with diabetes, gestational weight gain close to or slightly lower than the lower limits of the NAM guidelines seems therefore most appropriate, although randomised controlled trial data are absent.[40,48]

Pharmacological approaches

Antihypertensive treatment

Hypertensive disorders in pregnancy, such as chronic hypertension, pregnancy-induced hypertension (ie, developing after 20 weeks), and pre-eclampsia (ie, hypertension in combination with proteinuria or new onset of symptoms of maternal organ dysfunction after 20 weeks), affect up to 40% of pregnancies in women with type 1 diabetes.[54] High-diastolic blood pressure is the main, potentially modifiable predictor for pre-eclampsia in women with type 1 diabetes.[3] Pre-eclampsia in women with type 1 diabetes often develops before 37 weeks, leading to higher rates of preterm birth than when pre-eclampsia is not present.[55] Both elevated home and office blood pressure in early pregnancy are positively associated with the development of pre-eclampsia and are useful for prediction of pre-eclampsia in pregnant women with type 1 diabetes.[56] Several studies have shown that early and intensive antihypertensive treatment (ie, if blood pressure >135/85 mm Hg or urinary albumin excretion ≥300 mg per 24 h) in pregnant women with type 1 diabetes and diabetic kidney disease can reduce the prevalence of preeclampsia.[3,57–59] Angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers should be replaced before pregnancy due to possible teratogenic risk, with antihypertensive therapy approved for use in pregnancy.[60] Methyldopa is widely used, but the addition of labetalol or a calcium antagonist (ie, nifedipine or diltiazem) could be indicated to manage hypertension and albuminuria.[57,59,61]

Low-dose aspirin

Aspirin is often prescribed to pregnant women at increased risk of developing pre-eclampsia.[25] The largest randomised controlled trial assessing aspirin in pregnant women to date, the Aspirin for Evidence-Based Preeclampsia Prevention study,[62] showed that, compared with placebo, treatment with aspirin at 150 mg per day taken from 11–14 weeks until 36 weeks reduced the risk for preterm pre-eclampsia before 37 weeks with an OR of 0·38 in women at high risk for pre-eclampsia. However, less than 2% of the total study population had diabetes.[62] Only two smaller randomised controlled trials have investigated the use of aspirin in women with pregestational diabetes, showing no risk reduction for pre-eclampsia.[63,64] However, treatment with aspirin was mostly started in the second trimester, suggesting that aspirin therapy might be more beneficial if started early in gestation. A large, Danish, prospective cohort study showed that implementation of prophylactic aspirin for all pregnant women with type 1 diabetes and type 2 diabetes did not reduce the risk for pre-eclampsia compared with the previous risk-based prophylaxis strategy.[25] However, this study was not randomised and might have been underpowered. Therefore, evidence suggests that women with type 1 diabetes with additional risk factors, such as a previous history of pre-eclampsia, chronic hypertension, or diabetic kidney disease, should receive prophylactic aspirin starting before 16 weeks of pregnancy. However, given the scarcity of data, whether women with type 1 diabetes at low risk would equally benefit from the use of prophylactic aspirin in pregnancy is less clear. The IRELAND study[65] (EudraCT 2018-000770-29) is an ongoing randomised controlled trial investigating the potential benefit of low-dose aspirin in preventing pre-eclampsia in women with pregestational diabetes and will evaluate whether aspirin should be universally prescribed to women with pregestational diabetes in the first trimester of pregnancy.

Insulins for type 1 diabetes during pregnancy

In pregnant women with type 1 diabetes, insulin analogues are the first choice compared with human insulins because the fast-acting insulin analogues offer more flexibility and reduce the risk of hypoglycaemia and the long-acting insulin analogues are active for up to 24–42 h with lower risk of nocturnal hypoglycaemia.[66]

The short-acting insulin analogues, lispro and aspart, are approved for use in pregnancy and studies have shown similar achievement of glycaemic targets and pregnancy outcomes as regular human insulin.[67,68] The newer, ultra-rapid acting insulin formulations, rapid-acting aspart (Fiasp) and rapid-acting lispro (Lyumjev) have also received European approval for use in pregnancy as they only differ from their previous iterations by the addition of ingredients that are generally regarded as safe.[69,70] However, there is currently no evidence that these new formulations lead to increased time in range or improved pregnancy outcomes compared with rapid-acting inulin analogues. The results from a large randomised controlled trial (NCT03770767) comparing Fiasp to aspart in pregnancy are expected in 2023.[71] Glulisine is not approved for use in pregnancy due to an absence of data from large studies.[61,66] To account for increased post-meal insulin resistance and delayed insulin absorption with advancing gestation, the short-acting insulin analogues should be injected at least 15 min before meals in early pregnancy, extending to 30–45 min before meals in late gestation.[72]

A large randomised controlled trial has shown lower fasting glycaemia with the long-acting insulin analogue, insulin detemir, compared with neutral protamine Hagedorn insulin with similar HbA_{1c} and rates of hypoglycaemia.[73] There are no randomised controlled trials that use glargine in pregnancy, but both glargine

U100 and U300 are commonly used in pregnancy as observational data have not shown any safety issues.[66,74] A 2022 prospective cohort study showed that degludec resulted in similar metabolic control and pregnancy outcomes compared with glargine or detemir.[75] The multicentre randomised controlled trial (EXPECT[76]) in pregnant women with type 1 diabetes, comparing degludec with detemir (both in combination with insulin aspart), found degludec to be non-inferior to detemir with similar HbA_{1c} and pregnancy outcome. On the basis of this study, degludec is no longer contraindicated in pregnancy in Europe, the USA, and Canada.

The use of technology for glycaemic management

CGM in type 1 diabetes pregnancy

CGM technology has led to better management of type 1 diabetes, leading to less hypoglycaemia, lower HbA_{1c} concentrations, and improved treatment satisfaction.[77,78] Real-time CGM (rt-CGM) continuously collects glucose data and transmits them every 1–5 min to a receiver, insulin pump, or smartphone application, whereas intermittently scanned CGM (is-CGM) requires the patient to actively scan the sensor to view glucose concentrations.[79] Four randomised controlled trials have investigated the use of CGM compared with self-monitoring of blood glucose (SMBG) alone in women with type 1 diabetes in pregnancy (appendix p 2).[13,80–82] Two studies investigated intermittent use of a masked CGM in a mixed population, which included individuals with type 1 diabetes, type 2 diabetes, and, in one study, also including women with gestational diabetes, and showed conflicting results.[80,81] The first randomised controlled trial evaluating intermittent rt-CGM at five points during pregnancy showed no improvement in HbA_{1c} concentrations or improvement in pregnancy outcomes.[82] However rt-CGM was only used intermittently and only 49 (62%) of 79 participants used the rt-CGM as per protocol due to alarm fatigue or technical issues. Studies in non-pregnant adults have indicated that CGM use of at least 70–80% of the time is needed for optimal effects.[79]

The largest randomised controlled trial to date on CGM in pregnancy, the continuous glucose monitoring in pregnant women with type 1 diabetes (CONCEPTT) trial,[13] showed that the use of rt-CGM in addition to SMBG was associated with lower HbA_{1c} concentrations, higher TIR, and less glycaemic variability compared with SMBG alone. In addition, neonatal outcomes were improved, with reductions in LGA infants, NICU admissions for longer than 24 h, and neonatal hypoglycaemia requiring IV dextrose infusion (with a number to treat between 6–8).[13] Strengths of this study are the large sample size (325 participants) and the fact that randomisation was stratified according to the use of multiple daily injections (MDI), continuous subcutaneous insulin infusion therapy (CSII), and baseline HbA_{1c}. Moreover, only participants who showed sufficient compliance with CGM use were randomly assigned in the study. As only pregnant women with HbA_{1c} between 6·5% (48 mmol/mol) and 10·0% (86 mmol/mol) could participate, whether women with lower HbA_{1c} in early pregnancy, can also benefit from rt-CGM use remains less clear. The continuous glucose monitoring in pregnant women with type 1 diabetes (CONCEPTT) trial also showed that the use of CGM results in important cost savings in the UK, driven by fewer NICU admissions[83] and the potential to have improved neonatal outcomes at no increased costs when used in Canada.[84] Therefore, the diabetes guidelines in the UK and Canada recommend the use of rt-CGM for all pregnant women with type 1 diabetes.[85,86]

CGM systems approved for use in pregnancy are presented (table 1). There are currently no randomised controlled trial data on the use of is-CGM, such as the Freestyle Libre (Flash), on glycaemia and pregnancy outcomes in women with type 1 diabetes. A study in pregnant women with diabetes showed that, compared with SMBG, FreeStyle Libre 1 (FSL1) is safe to use in pregnancy with improved treatment satisfaction and similar accuracy irrespective of type of diabetes, pregnancy duration, or BMI.[87] Another study showed that FSL1 gave lower glucose estimates than SMBG in pregnancy.[88] In addition, simultaneously monitoring with FSL1 and rt-CGM for 7 days in early pregnancy showed that FSL1 measured more TBRp during the night time compared with rt-CGM.[89] Asymptomatic nocturnal hypoglycaemia measured by FSL1 should therefore not necessarily lead to insulin dose reduction or increased carbohydrate intake unless the hypoglycaemia is confirmed. A real-world cohort study comparing FSL1 to SMBG in type 1 diabetes pregnancies showed a transient lower HbA_{1c} in the second trimester, but more neonatal hypoglycaemia (27·4% *vs* 19·1%) in the infants of FSL1 users.[100] The reason is unclear, but FSL1 might have led to falsely lower glucose values, increasing the risk for suboptimal glycaemic management. The new versions of FSL (ie, the is-CGM FreeStyle Libre 2 and the rt-CGM FreeStyle Libre 3) have, in contrast to the first version, improved accuracy and optional alarms that warn the user of hypoglycaemia or hyperglycaemia.[101] Whether the frequent measurement of lower glucose values in pregnancy also occurs with the newer FSL versions is unclear.

In women with type 1 diabetes, higher mean CGM glucose profiles starting from 10 weeks gestation onwards are associated with LGA infants.[102,103] Along with higher HbA_{1c}, lower TIRp and higher time above range (TARp) were consistently predictive for obstetric and neonatal complications.[90,91,104] A Chinese study found a moderate correlation between HbA_{1c} and TIRp during pregnancy, suggesting that TIRp of at least 78% is needed to achieve a target HbA_{1c} of less than 6·0%.[105] In a US study, the correlation between HbA_{1c} and TIRp during the second and third trimesters was high, but lower in the first trimester. Moreover, the glucose management indicator (GMI; a mathematical formula to estimate

	Study results on pregnancy that are available	Studies on pregnancy that are ongoing	Approval outside pregnancy	Specific approval for pregnancy by European Conformity mark, year	Specific approval for pregnancy by FDA, year
CGM					
FreeStyle Libre 1 Flash glucose monitoring system (is-CGM without alarm function; Abbott Diabetes Care, Alameda, CA, USA)	FreeStyle Libre in pregnancy study (FLIPS, NCT02665455),[87] a prospective, single-arm study: n=74 (type 1 diabetes n=24, type 2 diabetes n=11, and GDM n=39). Clinical accuracy of Flash vs SMBG results was shown, with 88·1% of results within zone A (primary outcome) and and 99·8% of results within zones A and B of the consensus error grid at gestation of 26·6 ± 6·8 weeks. Overall mean absolute relative difference was 11·8%. Sensor accuracy was unaffected by type of diabetes, stage of pregnancy, age, or BMI. High satisfaction with sensor wear. Prospective, observational study[88] comparing Flash 1 with SMBG for 14 days in type 1 diabetes (n=25), insulin-treated women with type 2 diabetes (n=4), and GDM (n=4): at different timepoints of the day, 83–92% of discordant results were because of Flash values being lower than SMBG values. In patients requiring therapeutic changes to treat or prevent hypoglycaemia or hyperglycaemia, 25–35% of choices would have been divergent if based on Flash rather than SMBG (primary outcome). Prospective, observational study[89] in 20 women with type 1 diabetes, between 8–14 weeks gestation, monitored with Flash 1 and rt-CGM for 7 days simultaneously (Envision Pro Medtronic MiniMed, Northridge, CA, USA). Mean glucose for 24 h and overnight was similar between Flash and rt-CGM (p>0·050), but TBRp at night was higher with Flash (6·5% *vs* 0·0%, p=0·0030) and TIRp was lower with Flash (55·4% *vs* 68·8%, p=0·0050; primary outcomes).	Flash glucose monitoring in GDM: study protocol for a RCT (FLAMINGO, NCT04422821).	European Conformity mark since 2014 and approval by FDA in 2017	Approved, 2017	Not approved
FreeStyle Libre 2 Flash glucose monitoring system (is-CGM with alarm function)	..	..	European Conformity mark since 2018 and approved by FDA in 2020	Approved, 2018	Approved, 2023
FreeStyle Libre 3 Flash glucose monitoring system (rt-CGM)	..	..	European Conformity mark since 2020 and approved by FDA in 2022	Approved, 2020	Approved, 2023
Dexcom G5 (rt-CGM; Dexcom, San Diego, CA, USA)	Pilot prospective CGM quality improvement project in pregnancy (NCT02556554). Several prospective observational studies in which Dexcom G4 and G5 were used.[90–92]	..	European Conformity mark and approved by FDA since 2015	Not approved	Not approved
Dexcom G6 (rt-CGM)	Prospective observational study[93] in 32 pregnant women in second or third trimester (type 1 diabetes n=20, type 2 diabetes n=3, and GDM n=9). Each wore two G6 sensors on the abdomen, upper buttock, posterior upper arm, or in combination for 10 days and underwent a 6 h clinic session with YSI Analyzer (Xylem, Yellow Springs, OH, USA) reference blood glucose values obtained every 30 min. Compared with the reference blood glucose values, 92·5% of CGM values were within ±20% of paired reference values >100 mg/dL or ±20 mg/dL of YSI values ≤100 mg/dL. The MARD on the abdomen was 11·5%, upper buttock was 11·2%, and posterior upper arm was 8·7%.	Three studies in type 1 diabetes: AiDAPT RCT,[94] LOIS-P study (NCT04902378), and CIRCUIT RCT (NCT04492566). One study in type 2 diabetes (NCT05370612). Five studies in GDM (NCT05067075, NCT03981328, NCT04948112, NCT05430204, NCT05037526, NCT04605497). Three studies in pregestational diabetes and GDM: (NCT04605497, NCT04542148, NCT05492890).	European Conformity mark and approved by FDA since 2018	Approved, 2020	Not approved
Dexcom G7 (rt-CGM)	..	..	European Conformity mark and approved by FDA since 2022	Approved, 2022	Approved, 2022

(Table 1 continues on next page)

	Study results on pregnancy that are available	Studies on pregnancy that are ongoing	Approval outside pregnancy	Specific approval for pregnancy by European Conformity mark, year	Specific approval for pregnancy by FDA, year
(Continued from previous page)					
Dexcom One (rt-CGM, no connectivity with insulin pump)	..	..	European Conformity mark since 2022, but not approved by FDA	Not approved	Not approved
Medtronic Guardian 3 (rt-CGM; Medtronic, Northridge, CA, USA)	..	CRISTAL RCT (NCT04520971).[95]	European Conformity mark since 2017 and approved by FDA in 2018	Approved, 2017	Not approved
Medtronic Guardian 4 (rt-CGM)	..	CRISTAL RCT (NCT04520971).[95]	European Conformity mark since 2021, but not approved by FDA	Approved, 2021	Not approved
Pump					
Medtronic MiniMed 670G (by use of treat-to-target proportional integral derivative technology with insulin feedback with Guardian 3 CGM), non-customisable glucose target 6·7 mmol/L (120 mg/dL)	Case reports showed no safety events:[96] automatic mode started at 16 weeks gestation. TIRp increased from 46·8% to 51·3%.[97] HCL therapy throughout gestation, but with inconsistent time in automatic mode. Glycaemic control improved with time at <3·9 mmol/L (<70 mg/dL), 8–4% and time at 3·9–10·0 mmol/L (70–180 mg/dL) of 83–94%.[98] HCL therapy started in the second trimester, ASG concentrations of 7·0 ± 2·7 mmol/L in the second trimester before HCL use, 7·1 ± 2·1 mmol/L in the second trimester after HCL use, and 6·8 ± 1·9 mmol/L in the third trimester.	Pregnancy intervention with a closed-loop system RCT (NCT03774186).	European Conformity mark since 2018 and approved by FDA in 2016	Not approved	Not approved
Medtronic MiniMed 780G (by use of proportional-integral-derivative technology with insulin feedback with the most advanced SmartGuard technology, with Guardian 3 or 4 CGM), customisable glucose target 6·7 (120 mg/dL), 6·1 (110 mg/dL), or 5·5 mmol/L (100 mg/dL)	..	CRISTAL RCT (NCT04520971).[95]	European Conformity mark since 2020, but not approved by FDA	Not approved	Not approved
Tandem t:slim X2 with Control-IQ technology (treat-to-range predictive algorithm, currently with Dexcom G6 CGM; Tandem Diabetes Care, San Diego, CA, USA). Non-customisable target range options. Responsive to user basal rate and sensitivity adjustments. Sleep activity range 6·2–6·7 mmol/L (112·5–120 mg/dL), which can be used 24 h a day with optional exits to regular Control-IQ activity target range 6·2–8·9 mmol/L (112·5–160 mg/dL), or exercise activity range 7·8 to 8·9 mmol/L (140–160 mg/dL)	..	CIRCUIT RCT (NCT04902378).	European Conformity mark since 2018 and approved by FDA in 2019	Not approved	Not approved
CamAPS FX (Cambridge treat-to-target adaptive MPC; University of Cambridge, Cambridge, UK) DanaRS insulin pump (with Dexcom G6 CGM; SOOIL, Seoul, South Korea), personalised glucose target recommended setting 5·5 mmol/L (100 mg/dL) before 16 weeks gestation, and 4·5–5·0 mmol/L (81–90 mg/dL) from 16 weeks until delivery	..	AiDAPT RCT (NCT04938557).[94]	European Conformity mark since 2020, but not approved by FDA	Approved, 2020	Not approved
Pregnancy-specific zone-MPC based HCL algorithm (Harvard University) with the iAPS (Tandem Diabetes Care), glucose target 4·4–6·1 mmol/L (80–110 mg/dL) during the day and 4·4–5·5 mmol/L (80–100 mg/dL) during the night	First part LOIS-P consortium study (supervised setting).[19]	Second part LOIS-P consortium study (out-patient setting. NCT04492566).	Not approved	Not approved	Not approved
DBLG1 (a machine learning-based algorithm with Dexcom G6 CGM; Diabeloop, Grenoble, France), glucose target 6·1 (110 mg/dL), customisable between 5·5–7·2 mmol/L (100–130 mg/dL)	Case report showing successful management of pregnancy in a patient with highly unstable type 1 diabetes and hypoglycaemia unawareness by use of the closed-loop Diabeloop system for highly unstable diabetes.[99]	..	European Conformity mark since 2018, but not approved by FDA	Not approved	Not approved

(Table 1 continues on next page)

	Study results on pregnancy that are available	Studies on pregnancy that are ongoing	Approval outside pregnancy	Specific approval for pregnancy by European Conformity mark, year	Specific approval for pregnancy by FDA, year
(Continued from previous page)					
Omnipod 5 (SmartAdjust, with Dexcom G6 CGM; Insulet, Acton, MA, USA), glucose target 6·1 mmol/L (110 mg/dL, customisable)	..	..	European Conformity mark since and approved by FDA in 2022	Not approved	Not approved
Beta Bionics iLet Bionic Pancreas (with Dexcom G6 CGM; Beta Bionics, Irvine, CA, USA), glucose target 6·1 mmol/L (110 mg/dL)	..	..	Not yet approved	Not approved	Not approved
Inreda Diabetic Artificial Pancreas (dual hormone CL system; Inreda Diabetic, Goor, Netherlands), insulin delivery when >6·5 mmol/L (117 mg/dL)	..	..	European Conformity mark since 2020, but not approved by FDA	Not approved	Not approved

AiDAPT=automated insulin delivery amongst pregnant women with type 1 diabetes. ASG=average sensor glucose. CGM=continuous glucose monitoring. DBLG1=Diabeloop Generation 1. HCL=hybrid closed-loop. FDA=US Food and Drug Administration. GDM=gestational diabetes mellitus. is-CGM=intermittently-scanned CGM. iAPS=interoperable artificial pancreas system. LOIS-P=Longitudinal Observation of Insulin requirements and Sensor use in Pregnancy. MARD=mean absolute relative difference. MPC=model predictive controller. RCT=randomised controlled trial. rt-CGM=real-time CGM. SMBG=self-monitoring of blood glucose. TBR=time below range. TIR=time in range in pregnancy.

Table 1: **Approval of types of CGM and HCL technologies for use in pregnant women with type 1 diabetes**

HbA_{1c} from CGM glucose concentrations) had a high correlation with HbA_{1c} in all trimesters.[91]

The use of CGM also reduces fear of hypoglycaemia and improves detection of asymptomatic nocturnal hypoglycaemia.[92,106,107] CGM might also facilitate follow-up by telemedicine and lead to improved user experiences and easier provision of information to guide clinical decisions, but the evidence in pregnant women with type 1 diabetes is scarce.[108,109]

Use of insulin pump therapy

In high-income countries, between 30% and 90% of pregnant women with type 1 diabetes use insulin pumps to adapt to glycaemic variability in early pregnancy and to adjust for the increasing insulin doses later in pregnancy.[1,6,110] Still, meta-analyses, mostly including studies from before 2010, do not show better glycaemic management or improvement of pregnancy outcomes in women using CSII compared with MDI.[111–113] A retrospective study reported higher rates of LGA infants in women using insulin pumps than in women using MDI, possibly mediated by excess maternal weight gain, which was more frequent in those on CSII than in women on MDI.[114] Moreover, a secondary analysis of the CONCEPTT trial indicated that women on MDI more frequently kept to second trimester HbA_{1c} targets, with lower rates of gestational hypertension, neonatal hypoglycaemia, and NICU admissions compared with women on CSII.[115] The pregnancy outcomes were adjusted for important baseline maternal characteristics, including age and HbA_{1c}. The glycaemic differences in pump users were not explained by maternal dietary intake.[47] However, as women were not randomly assigned to MDI or CSII, preferences of participants and professionals for MDI or CSII might have led to residual confounding and whether pump treatment was optimally implemented was unclear. This finding suggests that frequent adjustments of insulin pump settings are necessary with more aggressive basal doses and premeal boluses, especially from mid-gestation onwards when insulin resistance increases.[116]

Sensor-augmented pump (SAP) therapy refers to the use of an insulin pump and a CGM simultaneously, either without connectivity between the two devices or with the connectivity that allows the pump to suspend basal insulin delivery for low sensor glucose concentrations. SAP therapy has the advantage that it can reduce the risk of hypoglycaemia as shown by studies in non-pregnant adults and children.[117–120] Although SAP therapy with low-glucose suspend technology can protect against hypoglycaemia in pregnant women with type 1 diabetes,[121,122] whether it can improve pregnancy outcomes compared with standard insulin pump therapy remains unclear. In addition, the increased time of insulin suspension associated with SAP therapy and low glucose suspend technology could theoretically lead to increased rebound hyperglycaemia and ketonaemia in pregnancy. A small

crossover randomised controlled trial in pregnant women with type 1 diabetes showed that, despite longer time periods with suspended insulin delivery when predictive low glucose suspend (PLGS) was used, there was no increased ketonaemia, with less time in hypoglycaemia, and similar TIR and treatment satisfaction compared with the use of the low glucose suspend.[123] This finding suggests that PLGS might be a safe option for pregnant women at high risk for hypoglycaemia, such as women with a recent history of severe hypoglycaemia or with impaired hypoglycaemia awareness.[8,9]

Management during delivery and early postpartum

Whether falling insulin requirements (ie, ≥20%) in late pregnancy are a warning sign of placental insufficiency or if they mainly reflect variations in normal physiology remains unclear. A 2022 observational study showed no association between a 30% decrease in insulin requirements with neonatal morbidity, although this finding might be because earlier delivery prevented these complications.[124] In general, guidelines recommend intrapartum capillary glucose concentrations of 4·0–7·0 mmol/L (70–126 mg/dL) in women with diabetes to reduce the risk for neonatal hypoglycaemia.[125,126] However, studies published more recently than these guidelines suggest that persistent maternal hyperglycaemia during second and third trimesters of pregnancy is strongly associated with neonatal hypoglycaemia, whereas a 5–7% TIR increase is associated with less neonatal hypoglycaemia.[126–128] Therefore, target glycaemic concentrations during labour and the delivery might not be able to reverse fetal hyperinsulinaemia.[129] The Joint British Diabetes Society for Inpatient Care has proposed a more pragmatic approach than the previous recommendations, with safer intrapartum glycaemic targets (5·0–8·0 mmol/L [90–144 mg/dL]) to facilitate self-management and reduce the risk of severe maternal hypoglycaemia.[126] Retrospective cohort studies have shown that continuation of intrapartum insulin pump therapy with CGM can be a safe option, without differences in the time spent in hypoglycaemia, whereas some studies showed improved glucose values in selected insulin pump users.[130,131] Given that insulin resistance drops immediately after delivery, the insulin doses should be reduced by at least 50% postpartum compared with late third trimester doses.[126] If women are breastfeeding, insulin requirements are approximately 20% lower than pre-pregnancy.[132–135] If insulin doses are reduced appropriately with sufficient carbohydrate intake during day-time, there is a low risk for night-time hypoglycaemia and carbohydrate intake at each night-time breastfeed is not always necessary.[133]

Use of HCL systems

HCL insulin delivery systems offer automated glucose-responsive basal insulin delivery. Some HCL systems also provide automated hyperglycaemia correction boluses, whereas others do not.[136] Outside pregnancy, HCL systems have led to a paradigm shift in the management of type 1 diabetes, with on average a 12% higher TIR (3·9–10·0 mmol/L [70–180 mg/dL]) compared with conventional pump therapy, with low risk of hypoglycaemia.[137,138]

CGM and insulin pumps are generally started before pregnancy to optimise preconception glycaemia and avoid the need to switch therapy during early pregnancy. Moreover, HCL systems are increasingly used as standard of care for the management of type 1 diabetes outside pregnancy and, given that unplanned pregnancies are still common, women might become pregnant while using these systems. In these cases, pregnant women and clinicians face the dilemma of whether they should switch to manual mode (ie, SAP therapy) or continue with HCL therapy. Some pumps (eg, Medtronic MiniMed; Medtronic, Northridge, CA, USA) might also allow the use of a suspend-on-low or PLGS instead of HCL with the same device if deemed beneficial for the individual. Other HCL systems (eg, Tandem Diabetes Care [San Diego, CA, USA] and Insulet [Acton, MA, USA]) offer SAP without insulin suspension or HCL within the same systems. These issues highlight the need for more evidence on the different HCL systems in pregnancy. An overview of the advantages and potential limitations of current HCL systems in pregnancy is provided (figure 2).

Studies with HCL systems in pregnancy

The first studies evaluating HCL insulin delivery in pregnant women with type 1 diabetes were performed more than 10 years ago in the UK. Two feasibility studies showed that a high TIR could be achieved safely and less time spent in extreme hypoglycaemia (table 2).[20,21] Two phase 2 pilot randomised controlled trials suggested proof of concept of HCL use in home settings (table 2). The first crossover randomised controlled trial showed that overnight HCL use was significantly more effective than SAP therapy with higher TIR.[22] A second crossover randomised controlled trial in a broader patient population, half of whom had HbA_{1c} of more than 7·5%, showed no significant differences in TIR between HCL and SAP therapy.[23] However, there was less time at less than 3·5 mmol/L (63 mg/dL) and less nocturnal hypoglycaemia during the use of HCL than during the use of SAP therapy. A secondary analysis of these two crossover randomised controlled trials reported that 84·4% of participants continued to use HCL intrapartum and postpartum, with a mean TIR of 82·0% during delivery and 83·3% postpartum.[139] In general, women expressed high degrees of trust in the HCL system, with feelings of improved glucose concentrations and increased peace of mind. However, women also reported concerns about CGM accuracy and burden of maintenance requirements.[140] Most women became more positive throughout pregnancy as their experience with using the HCL technology increased.[141] However, the study devices used 10 years ago were far less sophisticated than the

commercially available HCL systems today, which might have led to more burden with the devices.

A consortium from the USA designed a zone model predictive control (zone-MPC)-based, closed-loop system specifically customised for use in pregnancy, allowing for lower glycaemic targets than most comercially available HCL systems (4·4–6·1 mmol/L [80–110 mg/dL] during the day and 4·4–5·5 mmol/L [80–100 mg/dL] during the night).[142] The zone-MPC algorithm (Harvard University) runs on the interoperable artificial pancreas system (iAPS), which consists of the Dexcom G6 (Dexcom, San Diego, CA, USA), the Tandem t:AP research insulin pump, and an unlocked smartphone.[143] Meals need to be announced to the system by the user and meal boluses are calculated on the basis of the participants' prescribed bolus settings and user-estimated carbohydrate intake. In a pilot observational study,[19] 11 women with type 1 diabetes on SAP therapy switched to the HCL system for 2 days (table 2). Compared with the 1 week run-in period with SAP therapy, TIR was higher with the HCL system with less time in hypoglycaemia.[19]

Several larger and longer multicentre trials examining the clinical efficacy and safety of HCL systems in pregnant women with type 1 diabetes are currently ongoing or have been recently completed (table 3). The Pregnancy Intervention With a Closed-Loop System study is a pilot randomised controlled trial investigating the first commercially available HCL system, Medtronic 670G, compared with SAP therapy in pregnant women with type 1 diabetes. The limitation of the 670G system is that it uses an algorithm to target on average glucose of 6·7 mmol/L (120 mg/dL), which is not customisable to lower glucose concentrations and is higher than the recommended target for overnight use in pregnancy.[144]

The Automated insulin Delivery Amongst Pregnant women with Type 1 diabetes (AiDAPT) trial is the largest randomised controlled trial on HCL in pregnant women with type 1 diabetes and investigates the CamAPS (University of Cambridge, Cambridge, UK) with Dexcom G6 compared with standard of care (ie, pump or MDI).[94] The CamAPS is the first HCL system specifically licensed in 13 countries for use in pregnancy (eg, the UK, other European countries, and Australia; table 1). The CamAPS is compatible with several insulin pumps (mylife YpsoPump [Ypsomed, Burgdorf, Switzerland], DANA Diabecare RS [SOOIL, Seoul, South Korea], and DANA-I [SOOIL, Seoul, South Korea]) and with the Dexcom sensors (G6, G7) and FreeStyle Libre 3,[145,146] and both rapid and ultra-rapid insulin analogues can be used.[147] In contrast to other available commercial HCL systems, the CamAPS offers fully customisable glucose targets (4·4–11·1 mmol/L [80–200 mg/dL]). The lower limit of target glucose means that CamAPS is particularly applicable for use during pregnancy, when targets are typically set at 5·5 mmol/L (100 mg/dL) during the first trimester and 5·0 mmol/L (90 mg/dL) thereafter (table 1).

Several next-generation HCL systems (eg, the Tandem t:slim X2 with Control IQ, the Medtronic 780G, and DBLG1 [Diabeloop, Grenoble, France] systems) received approval in non-pregnant adults in 2020,[148–150] but are currently not approved for use in pregnancy (table 1). These HCL systems allow for a lower glucose target set (lowest target of 5·5 mmol/L [100 mg/dL] for the Medtronic 780G, 6·2–6·7 mmol/L (112·5–120 mg/dL) for the Tandem t:slim X2 with Control IQ, and 6·1 mmol/L [110 mg/dL] for DBLG1 and Insulet Omnipod 5), which might potentially lead to improved glycaemia compared with the 670G and 770G systems. The 780G system uses an algorithm that automatically adapts the basal rate and provides automated hyperglycaemia correction boluses. This type of HCL system might be particularly useful for women who prefer a HCL without the need for much intervention. In contrast, with the Tandem t:slim X2 with Control IQ, the basal rate and insulin sensitivity can be adapted, which might be a good option for women who prefer a HCL system that is less automated and allows for more personal intervention than the Medtronic 780G system. The closed-loop insulin delivery in pregnant women with type 1 diabetes (CRISTAL) study is the second largest randomised controlled trial comparing the Medtronic 780G system with standard of care.[144] The closed-loop Insulin delivery by glucose Responsive Computer algorithms In Type 1 diabetes pregnancies (CIRCUIT) study compares the Tandem t:slim X2 pump with Control IQ and Dexcom G6 versus standard of care with a Dexcom G6 sensor. Although the AiDAPT and CIRCUIT studies compare HCL to standard of care by use of the Dexcom G6 sensor, the CRISTAL study allows

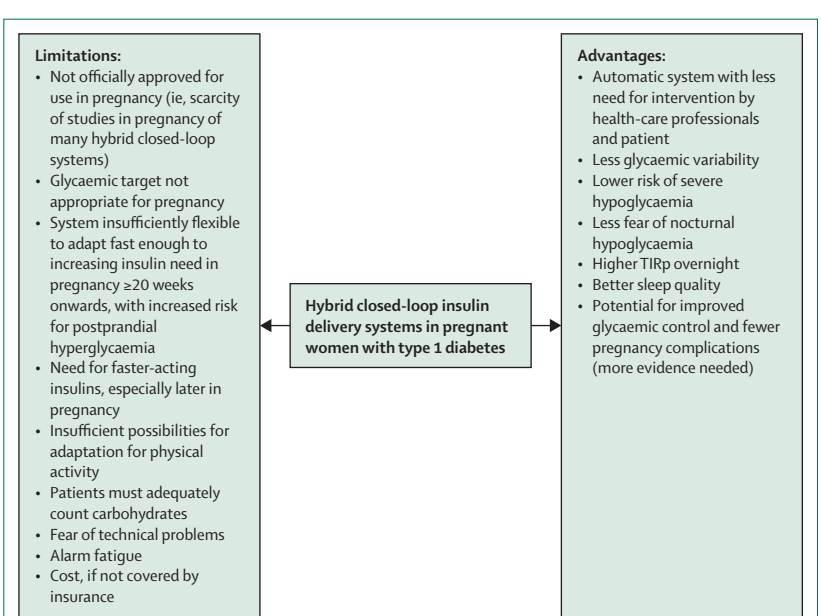

Figure 2: **Potential limitations of available HCL insulin delivery systems in pregnancy in women with type 1 diabetes and the advantages over the use of non-closed-loop CSII or MDI**
TIRp=time in range in pregnancy.

	Type of HCL	Study design	Primary outcome	Main results
Murphy et al, 2011;[20] UK (ISRCTN62568875)	Insulin pump (Deltec Cozmo; Smiths Medical, St Paul, MN, USA) with a MPC algorithm and FreeStyle Navigator CGM sensor (Abbott Diabetes Care, Alameda, CA, USA).	Phase 1a exploratory safety study, type 1 diabetes n=10, HbA1c ≤86 mmol/mol (≤10%), in which HCL insulin delivery was evaluated over 24 h in early (12–16 weeks) and late pregnancy (28–32 weeks) in a supervised hospital, clinical research-facility setting.	Mean glucose, TIRp 3·5–7·8 mmol/L (63–140 mg/dL), TBR <3·5 mmol/L (<63 mg/dL), TAR >7·8 mmol/L (>140 mg/dL), and insulin infusion rate measured at each visit with plasma and sensor glucose measurements.	Clinically and statistically acceptable accuracy of the FreeStyle Navigator CGM and Florence D2A MPC algorithm (University of Cambridge) in pregnant women with type 1 diabetes. During HCL, plasma glucose concentrations were 6·5 mmol/L (117 mg/dL) in early pregnancy and 7·0 mmol/L (126 mg/dL) in late pregnancy (p=0·72). HCL was associated with near normoglycaemia overnight, both in early (84%) and in late (100%) pregnancy (p=0·090), with overnight TAR of 7% and 0% and TBR of 0% and 0% in early and late pregnancy (p>0·050), respectively. Postprandial glucose control, glucose variability, insulin infusion rates, and CGM sensor accuracy were similar in early or late pregnancy, suggesting the MPC algorithm safely adapted insulin delivery for advancing gestational age.
Murphy et al, 2011;[21] UK (ISRCTN50385583)	FreeStyle Navigator CGM sensor with an intravenous sampling catheter and study pump (Animas 2020; Johnson and Johnson, New Brunswick, NJ, USA). HCL: Cambridge MPC algorithm.	Phase 1b randomised crossover trial with 12 pregnant women with type 1 diabetes, median HbA1c 46 mmol/mol (6·4%), comparing HCL with conventional CSII at two 24 h visits, separated by a 1–6 week interval (at 19 and 23 weeks).	Plasma glucose TIRp 3·5–7·8 mmol/L (63–140 mg/dL) from 1400 h on day 1 to 1230 h on day 2.	Plasma glucose TIRp was similar for HCL and conventional CSII (81% *vs* 81%, p=0·75) with less time spent extreme hypoglycaemic <2·5 mmol/L (<45 mg/dL. 0·0% *vs* 0·3%, p=0·040) and with a lower LBGI (2·4 *vs* 3·3, p=0·030) during HCL insulin delivery.
Stewart et al, 2016;[22] UK (ISRCTN71510001)	DANA Diabecare R Insulin Pump (SOOIL, Seoul, South Korea) and the FreeStyle Navigator II (Abbott Diabetes Care, Alameda, CA, USA). HCL: Cambridge MPC algorithm.	Phase 2, open-label, multicentre, randomised crossover study comparing overnight HCL therapy with SAP therapy, each used for 4 weeks in 16 pregnant women with type 1 diabetes, followed by a continuation phase in which the HCL system was used day and night until delivery in 14 pregnant women with type 1 diabetes.	Overnight TIRp 3·5–7·8 mmol/L (63–140 mg/dL), as recorded by means of CGM during each 4-week study phase.	Overnight HCL therapy resulted in higher TIRp than SAP therapy (74·7% *vs* 59·5%, p=0·0020). During the continuation phase (ie, up to 14·6 additional weeks, including antenatal hospitalisations, labour, and delivery), glucose concentrations were in the target range 68·7% of the time throughout pregnancy.
Stewart et al, 2018;[23] UK (ISRCTN83316328)	CGM (FreeStyle Navigator II; Abbott Diabetes Care, Alameda, CA) and insulin pump (DANA Diabecare R) with control Florence D2A MPC algorithm.	Phase 2, open-label, randomised, two-period crossover study in 16 pregnant women with type 1 diabetes (GA 8–24 weeks, with HbA1c ≥48 to ≤86 mmol/mol [≥6·5 to ≤10%]), 28 days of day and night HCL, and SAP insulin delivery separated by a washout period. Continuation phase possible up to 6 weeks postpartum.	TIRp 3·5–7·8 mmol/L (63–140 mg/dL) as measured by CGM during the 4-week intervention periods.	HCL insulin delivery was associated with comparable glucose concentrations (TIRp: 62·3% *vs* 60·1%, p=0·47) and significantly less hypoglycaemia than SAP therapy (<3·5 mmol/L [<63 mg/dL]. 1·6% *vs* 2·7%, p=0·020), less nocturnal hypoglycaemia (2300–0700h. 1·1% *vs* 2·7%, p=0·0080) and a trend toward higher overnight time in target (67·7% *vs* 60·6%, p=0·060).
Stewart et al, 2018;[139] UK (ISRCTN71510001 and ISRCTN83316328)	CGM (FreeStyle Navigator II), insulin delivery was through a DANA Diabecare R pump and the closed-loop systems used were the Florence D2W (on a tablet computer; University of Cambridge) and Florence D2A (on an Android smartphone).	Secondary analyses of all women included in the two randomised crossover trials who chose to continue to use closed-loop intrapartum and immediate postpartum period (27 [84·4%] of the potential 32 trial participants).	TIRp 3·5–7·8 mmol/L (63–140 mg/dL) during pregnancy and 3·9–10 mmol/L (70–180 mg/dL) immediately after delivery.	Use of HCL was associated with TIRp 82·0% (IQR 49·3–93·0) during labour and delivery and a mean glucose of 6·9 ± 1·4 mmol/L (124 ± 25 mg/dL). HCL performed well throughout vaginal, elective, and emergency caesarean section deliveries. Postpartum TIR was 83·3% (IQR 75·2–94·6), with a mean glucose of 7·2 ± 1·4 mmol/L (130 ± 25 mg/dL). There was no difference in maternal intrapartum glucose concentration between mothers of infants with (6·9 ± 1·6 mmol/L [124 ± 29 mg/dL]) and without neonatal hypoglycaemia (6·8 ± 1·1 mmol/L [122 ± 20 mg/dL], p=0·84).
Ozaslan et al, 2022;[19] USA (NCT04492566)	CGM, Dexcom G6 (Dexcom, San Diego, CA, USA) and a research insulin pump (Tandem Diabetes Care, San Diego, CA, USA) with zone-MPC algorithm (Harvard University). The devices are connected wirelessly to the iAPS installed on an unlocked smartphone	Multicentre pilot study evaluating the feasibility of closed-loop insulin delivery with a pregnancy-specific zone-MPC algorithm (iAPS running on an unlocked smartphone) in 11 pregnant women with type 1 diabetes, from gestational age 14–32 weeks, who were already using CGM augmented pump therapy. Consisting of up to 2 weeks run-in with participants with the study CGM and personal insulin pump therapy at home, followed by a 2-day HCL insulin delivery period in a supervised outpatient setting.	TIRp 3·5–7·8 mmol/L (63–140 mg/dL) compared with participants' 1-week run-in period.	Use of the pregnancy-specific zone-MPC was feasible in pregnant women with type 1 diabetes. Compared with the 1-week run-in, there was an increased TIRp during supervised HCL (81·5% *vs* 64%, p=0·0070) with less TAR (16·5% *vs* 30·8%, p=0·029) and TBR (2·0% *vs* 5·2%, p=0·039). Overnight glucose control was similar, except for less time >13·9 mmol/L (>250 mg/dL, 0% *vs* 3·9%, p=0·030) and lower glucose SD (1·3 mmol/L [23·8 mg/dL] *vs* 2·4 mmol/L [42·8 mg/dL], p=0·0070) during HCL.

HCL=hybrid closed-loop. MPC=model predictive controller. CGM=continuous glucose monitoring. TIRp=time in pregnancy range. TBR=time below range. TAR=time above range. CSII=continuous subcutaneous insulin infusion. LBGI=low blood glucose index. SAP=sensor-augmented pump. TIR=time in range. iAPS=interoperable artificial pancreas system

Table 2: **Results of the pilot HCL studies in pregnant women with type 1 diabetes**

	Type of HCL *vs* comparator	Countries and number of centres	Study design	Primary outcomes	Main secondary outcomes	Start date and study end
Pregnancy Intervention with a Closed-Loop System study (NCT03774186)	MiniMed 670G (Medtronic; Northridge, CA, USA) HCL with a proportional integral derivative algorithm and Guardian CGM system (Medtronic) *vs* sensor-augmented pump therapy (pump + non-communicating Guardian CGM system)	USA, 2 centres	Two-centre, prospective, open-label, single-blind, investigator-initiated, pilot RCT. 1:1 randomisation gestational age of 14–18 weeks. N=24 (12 per arm; up to 37 enrolled, but aimed for 20 completers [10 per group]). Eligibility was women of gestational age ≤11 weeks, HbA_{1c} 37–75 mmol/mol (5·5–9%), aged 18–45 years, type 1 diabetes diagnosis >1 year before, undergoing intensive insulin therapy (ie, MDI or CSII). Run-in phase of 7 days with CGM. Followed up until 4–6 weeks postpartum.	Number of severe hypoglycaemic episodes. Time <3 mmol/L (<54 mg/dL). CGM metrics: time <3·5 mmol/L (<63 mg/dL), 3·5–7·8 mmol/L (63–140 mg/dL), >7·8 mmol/L (>140 mg/dL) and >10 mmol/L (>180 mg/dL). Fear of hypoglycaemia, assessed with hypoglycaemia fear survey II.	Diabetic ketoacidosis, adverse skin reactions, mean glucose ± SD, J-index, high blood glucose index, LBGI, duration of hypoglycaemic episodes, mean amplitude of glycaemic excursions, continuous overall net glycaemic action, health status (assessed with SF-36), device satisfaction (assessed with INSPIRE, Insulin Delivery Satisfaction Survey, and Glucose Monitoring Satisfaction Survey), preeclampsia or eclampsia, caesarean sections, average gestational weight gain, miscarriage or stillbirth, LGA babies, and neonatal hypoglycaemia.	March, 2019–March, 2022
AiDAPT study (ISRCTN56898625)[94]	CamAPS FX AiD (CamDiab; Cambridge, UK) consisting of an insulin pump (Dana Diabecare RS, SOOIL; Seoul, South Korea), Dexcom G6 CGM system (Dexcom; San Diego, CA, USA), and computer-based MPC algorithm *vs* CSII or MDI without AiD and with Dexcom G6 CGM system	UK, 9 centres	Multicentre, open-label, two-arm, parallel group RCT. N=124 (62 per arm). 1:1 randomisation with stratification by site. Eligibility: viable pregnancy of gestational age <14 weeks, HbA_{1c} ≥48 mmol/mol (≥6·5%) at booking and ≤86 mmol/mol (≤10%) at randomisation, 18–45 years, type 1 diabetes diagnosis ≥1 year, intensive insulin therapy (≥3 injections/day or pump). Run-in phase of masked Dexcom G6 for baseline data collection (except for participants already using Dexcom G6 before enrolment). Study extended with 6 months postpartum follow-up.	TIRp 3·5–7·8 mmol/L (63–140 mg/dL) between 16 weeks until delivery.	HbA_{1c}, diabetic ketoacidosis, severe hypoglycaemia episodes, number and severity of episodes of adverse device effect, hospital length of stay (maternal), mode of delivery, gestational age at delivery, infant birth weight, LGA, SGA, neonatal morbidity, NICU admission, pregnancy loss <24 weeks, stillbirth, neonatal death, fear of hypoglycaemia (assessed with HFS-II, worry scale only), health status (assessed with EQ-5D-5L), diabetes distress (assessed with Diabetes Distress Scale), sleep quality (assessed with PSQI), device satisfaction (assessed with INSPIRE), qualitative interviews on diabetes management, expectations and experiences, and cost-effectiveness.	Jan, 2018–Nov, 2022
CRISTAL study (Closed-loop insulin delivery in pregnant women with type 1 diabetes; NCT0452097)[144]	MiniMed 780G system (Medtronic) with Medtronic Guardian 3 or 4 CGM system *vs* continue SoC (MDI or open-loop pump) with any type of sensor (blinded Guardian 3 CGM on top of sensor if no Guardian sensor at run-in, gestational age 14–17, 20–23, 26–29, and 33–36 weeks)	Belgium, 11 centres and Netherlands, 1 centre	Multicentre, open-label RCT. N=95 (47 per arm). 1:1 randomisation with stratification by centre, HbA_{1c} (<7% or ≥7%), and treatment (pump or MDI), gestational age <14 weeks. Eligibility: viable singleton pregnancy gestational age <12 weeks, HbA_{1c} ≤86 mmol/mol (≤10%) at booking, 18–45 years of age, type 1 diabetes diagnosis ≥1 year, intensive insulin therapy (MDI or pump). Run-in phase of 10 days with masked Guardian 3 CGM (not for participants already using Guardian 3 or 4 CGM before enrolment).	TIRp 3·5–7·8 mmol/L (63–140 mg/dL) at GA 14–17, 20–23, 26–29, 33–36 weeks.	Prespecified: time at <3·5 mmol/L (<63 mg/dL), overnight time at <3·5 mmol/L (<63 mg/dL), and overnight (midnight till 6 am) TIRp 3·5–7·8 mmol/L (63–140 mg/dL). Exploratory: device deficiencies, TIRp during the day, TIRp and HbA_{1c} during each trimester, mean glucose, time at >7·8 mmol/L (>140 mg/dL), time at >10·0 mmol/L (>180 mg/dL), time at <2·8 mmol/L (<50 mg/dL), time at 3·0 mmol/L (<54 mg/dL), LBGI, glycaemic variability, time in nonpregnant target range, severe hypoglycaemias, diabetic ketoacidosis, miscarriage, stillbirth, neonatal death, LGA, respiratory distress, birth trauma, shoulder dystocia, neonatal hypoglycaemia, NICU admission, general habits and socioeconomic background (assessed with a self-designed questionnaire), fear of hypoglycaemia (assessed with HFS-II), health status (assessed with SF-36), symptoms of clinical depression (assessed with 20-item Center for Epidemiologic Studies–Depression scale), diabetes-related emotional distress (assessed with Problem Areas in Diabetes–short form questionnaire), treatment satisfaction (assessed with Diabetes Treatment Satisfaction Questionnaire status and change), consumption of food and beverages (assessed with Food Frequency Questionnaire), skinfold thickness, cord blood C peptide, and cost-effectiveness.	Jan, 2021–May, 2023

(Table 3 continues on next page)

	Type of HCL *vs* comparator	Countries and number of centres	Study design	Primary outcomes	Main secondary outcomes	Start date and study end
(Continued from previous page)						
CIRCUIT study (NCT04902378)	Tandem t:slim X2 (Tandem Diabetes Care; San Diego, CA, USA) pump with control IQ (commercially available) with Dexcom G6 CGM system *vs* standard-of-care (MDI or pump) with Dexcom G6 CGM system	Canada, 9 centres	RCT. N=66. No stratification at randomisation. Eligibility: viable singleton pregnancy gestational age <14 weeks, HbA_{1c} ≥48 mmol/mol to <86 mmol/mol (≥6·5 to <10%), 18–45 years of age, type 1 diabetes diagnosis ≥1 year, and intensive insulin therapy (≥3 injections per day or CSII). Run-in phase of one week with Dexcom G6 CGM with 80% baseline capture.	TIRp 3·5–7·8 mmol/L (63–140 mg/dL) gestational age 16–34 weeks.	TBR, TAR, mean blood glucose, severe hypoglycaemia, diabetic ketoacidosis, proportion with maternal hypoglycaemic events, coefficient of variation, SD, diabetes-related distress (assessed with Diabetes Distress Screening Scale), fear of hypoglycaemia (assessed with HFS-II), fear of hyperglycaemia (assessed with Hyperglycaemia Fear in Pregnancy Survey), sleep quality (assessed with a modified PSQI), health status (assessed with EQ-5D-5L), work productivity (assessed with Work Productivity and Activity Impairment survey, diabetes-related distress to partners (assessed with Partner Diabetes Distress Scale), preeclampsia, gestational hypertension, worsening chronic hypertension events, caesarean sections, preterm delivery, LGA, SGA, mean neonatal birthweight, birthweight z-score, neonatal hypoglycaemia, NICU admission, pregnancy loss (stillbirth ≥20 weeks, neonatal loss up to 28 days) or miscarriage (<20 weeks), and device-related adverse events.	June, 2021–Jan, 2024
LOIS-P consortium (Automated Insulin Delivery in Pregnant Patients with Type 1 Diabetes with Extension into Outpatient at Home. NCT04492566)	AiD iAPS for pregnant women (pregnancy-specific zone-MPC algorithm [Harvard University] on an Android smartphone, Tandem research pump, and Dexcom G6: target 4·4–6·1 mmol/L [80–110 mg/dL] during the day and 4·4–5·6 mmol/L [80–100 mg/dL] 0000–0400 h).	USA, 3 centres	Observational safety and feasibility study (single-arm). N=10. At-home use of the system for 4 weeks with the option of continuing throughout pregnancy. Eligibility: women of gestational age 14–32 weeks, HbA_{1c} ≤85 mmol/mol (≤9·0%), 18–45 years of age, type 1 diabetes diagnosis >1 year, and insulin pump use. A 48–60 h HCL session in a supervised outpatient environment before participants take the system home.	TIRp 3·5–7·8 mmol/L (63–140 mg/dL) from start of the trial (second trimester) until end of system use (up to the end of pregnancy).	Overnight (0000-0600 h) TIRp, 2 h postprandial TIRp, glucose <3·5 mmol/L (<63 mg/dL), <3 mmol/L (<54 mg/dL), >7·8 mmol/L (>140 mg/dL), >10 mmol/L (>180 mg/dL), hypoglycaemic events, severe hypoglycaemic events, hyperglycaemic events, glucose >13·9 mmol/L (>250 mg/dL), serious adverse events, adverse device events, serious adverse device events, unexpected adverse device events, mean CGM glucose concentration, and number of hypoglycaemia treatments.	June, 2021–Dec, 2022
CLIMB study (NCT04420728)	Medtronic MiniMed 670G or 770G system with CGM with early (6–10 days postpartum) *vs* delayed (12 weeks postpartum) auto mode enabled (ie, HCL) insulin delivery.	Canada, 4 centres	Parallel, two-group, open-label, pilot RCT. N=20. Randomisation after birth (participants switched to automatic mode or continued to use the MiniMed 670G or 770G insulin pump in manual mode. Eligibility: viable singleton pregnancy, gestational age 12–32 weeks that are not planning to conceive another pregnancy in the first 24 weeks postpartum, HbA_{1c} <85 mmol/mol (<9·9%), 18–45 years of age, type 1 diabetes diagnosis ≥2 years, and intensive insulin therapy (≥3 injections per day or pump).	Effect of automatic *vs* manual mode of MiniMed 670G or 770G on TIR 3·9 to 10 mmol/L (70–180 mg/dL) 12 weeks postpartum.	TBR, TAR, glycaemic variability, diabetes-related distress (assessed with Diabetes Distress Scale 3), fear of hypoglycaemia (assessed with HFS-II), sleep quality (assessed with PSQI), intervention acceptability (assessed via qualitative interviews), intervention feasibility (assessed via study recruitment), retention and completion rates, and infant feeding practices (assessed with Child Food and Liquid Intake Questionnaire).	July, 2020–March, 2023

AiD=automated insulin delivery. AiDAPT=Automated insulin Delivery Amongst Pregnant women with Type 1 diabetes. CGM=continuous glucose monitoring. CIRCUIT=Closed-loop Insulin delivery by glucose Responsive Computer algorithms In Type 1 diabetes pregnancies. CLIMB=Closed-Loop Insulin delivery postpartum in Mothers with type 1 diabetes and their Babies' feeding practices. CSII=continuous subcutaneous insulin infusion. EQ-5D-5L=EuroQol five-dimensions health-related quality of life questionnaire. GMSS=glucose monitoring satisfaction survey. HCL=hybrid closed-loop. HFS-II=hypoglycaemia fear survey II. iAPS=interoperable artificial pancreas system. INSPIRE=Insulin dosing Systems: Perceptions, Ideas, Reflections, and Expectations. LBGI=low blood glucose index. LGA=large for gestational age. MDI=multiple daily injections. MPC=model predictive controller. NICU=neonatal intensive care unit. PSQI=Pittsburgh sleep quality index. RCT=randomised controlled trial. SF-36=36-Item Short Form Health Survey. SGA=small for gestational age. TAR=time above range. TBR=time below range. TIR=time in range. TIRp=time in range in pregnancy. UADE=unanticipated adverse device effects.

Table 3: **Characteristics of ongoing, larger HCL studies in pregnant women with type 1 diabetes**

for the use of all types of glucose sensors in line with routine care and has no lower limit in HbA_{1c} for inclusion, therefore also evaluating women with near-target glucose concentrations (table 3). The observational study of the Longitudinal Observation of Insulin requirements and Sensor use in Pregnancy (LOIS-P) consortium evaluates the home use of the iAPS with a pregnancy-specific zone-MPC algorithm. Given that this algorithm allows for lower glycaemic targets (4·4–6·1 mmol/L [80–110 mg/dL] during the day and 4·4–5·5 mmol/L [80–100 mg/dL] during the night) compared with the commercially available Tandem t:slim X2 pump with Control IQ, this technology might be particularly useful for the more strict glycaemic targets needed in pregnancy.

The sample size of the studies is powered for primary maternal glycaemic efficacy outcome, such as the percentage TIRp. Secondary outcomes include severe hypoglycaemia and diabetic ketoacidosis, adverse events, obstetric and neonatal outcomes, and participant-reported outcomes (eg, treatment satisfaction, general health status, and fear for hypoglycaemia). These studies will report on whether HCL systems can improve glycaemic management in type 1 diabetes pregnancies. Several studies will also investigate the cost-effectiveness of HCL systems in pregnancy.[94,95] However, given that none of these individual studies are powered for pregnancy outcomes, we have established an international collaborative network to perform a meta-analysis to evaluate the effect of HCL use on obstetric and neonatal outcomes. In addition, as participant-reported outcomes should be prioritised and considered as equally important as glycaemic outcomes, this meta-analysis will also include participant-reported outcomes to identify the psychosocial effect of HCL use in pregnancy. To facilitate the real-world adoption of HCL systems in pregnant women with type 1 diabetes, presenting HCL to pregnant women and health-care professionals as a pillar of a three-party collaboration might help to promote optimal use.[151] However, for broad implementation of HCL use in pregnancy, improved equity in access to HCL systems worldwide is also needed.

The international consensus on TIR[15] does not recommend specific TIRp according to the different trimesters. However, as is the case for guidelines related to blood glucose targets in pregnancy, in women with severe hypoglycaemia more relaxed TIRp targets (eg, 60% TIRp rather than 70%) might be needed for safety. Moreover, the currently recommended TIRp does not distinguish between glucose target overnight compared with the daytime. Studies with HCL systems (both in non-pregnant adults and children as in pregnant women) have shown that a higher TIR of approximately 75% is achievable overnight compared with during the daytime.[22,137,138] Data coming from the larger studies on HCL systems in pregnancy might inform more specific recommendations concerning the targets for TIRp in the different trimesters and overnight. Adapted recommendations might be needed concerning the timing of the bolus before meals when HCL systems are used in pregnancy. Due to the automatic adaptation of the basal rate, bolus should be given a minimum of 10–15 min before meals, and there might be less of a need to administer the bolus 30–45 min before meals in late pregnancy, as recommended when MDI or insulin pumps are used, although response should be individualised on the basis of each woman and system used.

Psychosocial experiences

Pregnancy is often a time of heightened anxiety, which might be especially applicable for women with type 1 diabetes as they are advised to consistently achieve blood glucose concentrations in the pregnancy target range even before becoming pregnant and to maintain this target throughout pregnancy. A qualitative study reported significant impairment of psychological health and overall quality of life in women with type 1 diabetes who were pregnant or planning pregnancy. Most women reported a lack of support and empathetic engagement from their health-care team, which affected their clinical management. Barriers for optimal management included guilt and concerns about high blood glucose concentrations, constant pressure to meet glucose targets, and difficult interactions with health-care professionals.[152] Effective clinical and psychosocial support for pregnant women with type 1 diabetes is therefore needed.

Conclusion

Glycaemic management in type 1 diabetes pregnancy remains challenging with an increased risk of pregnancy complications. In addition, a holistic approach is necessary with considerations for lifestyle and psychosocial support alongside the use of modern technology to maintain target glycaemia. Diabetes technology, including CGM, insulin pumps, and newly developed HCL systems,

Search strategy and selection criteria

We searched PubMed for articles published between Jan 1, 2000, and March 28, 2023, using the search terms "continuous glucose monitoring", "flash glucose monitoring", "insulin pumps", "sensor-augmented pump therapy", "closed-loop therapy", "closed-loop insulin delivery", "CSII", "automated insulin delivery", "HbA_{1c}", "glycaemic control", "hypoglycaemia", "glycaemic variability", "time-in-range", "predictive low glucose suspend", "pregnancy outcomes", "delivery", "breastfeeding", "postpartum", "lifestyle", "diet", "gestational weight gain", "blood pressure control", "hypertension", "low-dose aspirin", in combination with the terms "type 1 diabetes" and "pregnancy". A literature search strategy was developed by combining the different medical subject headings, applied as: concept 1 (type 1 diabetes) AND concept 2 (pregnancy) AND in combination with other consecutive search terms added with OR.

hold promise in the management of type 1 diabetes in pregnancy. Given that avoiding hypoglycaemia alone is not enough to reduce the risk for pregnancy complications, HCL systems might help to maximise TIRp and, as such, improve obstetric and neonatal outcomes. The effect of HCL systems on pregnancy outcomes should be explored in a meta-analysis, which would help to guide clinicians and women with type 1 diabetes on the use of new diabetes technology in pregnancy.

Contributors

All authors were responsible for the conceptualisation and methods of the review. KBen was responsible for the original draft of this Review. KBeu and KBen created the tables and figures and performed the literature search, and all authors reviewed and edited the manuscript.

Declaration of interests

KBen reports research funding and receipt of study devices from Medtronic for the investigator-initiated CRISTAL study, receipt of study devices from Dexcom, received consulting fees from AstraZeneca and Eli Lilly, and served on the speaker bureau for Novo Nordisk, AstraZeneca, and Mundipharma. SP reports grants from Dexcom and National Institute of Health (NIH), research support from Medtronic, and payment from diaTribe for an online article and participation on a DSMB from Sansum Diabetes Research Institute. LED reports grants from Diabetes Canada, Calgary Health Trust and Alberta Diabetes Institute, and in-kind, reduced cost, and loan of study devices from Medtronic, Dexcom, and Tandem Diabetes Care. CJL reports grants from the Helmsley Foundation, NIH (1R01DK120358–0), Tandem, Dexcom, Insulet, and Abbott Diabetes. CM reports consulting fees from Novo Nordisk, Sanofi, Merck Sharp and Dohme, Eli Lilly, AstraZeneca, Boehringer Ingelheim, Roche, Medtronic, ActoBio Therapeutics, Pfizer, Insulet, and Zealand Pharma, and serves or has served on the speaker bureau for Novo Nordisk, Sanofi, Eli Lilly, Boehringer Ingelheim, AstraZeneca, and Novartis. DSF reports grants from the Canadian Institute for Health Research; in-kind, reduced cost, and loan of study devices from Tandem Diabetes Care and Dexcom; has served on an advisory board for Novo Nordisk; and received honoraria from Sanofi and Novo Nordisk. RP reports multiple grants from ZonMw and Leading the Change (Netherlands governmental health-care research funds). SES has made webinars and a podcast on time in range and diabetes in pregnancy in cooperation with Abbott Diabetes, Medtronic, Eli Lilly, and Sanofi, and has served in advisory boards from Novo Nordisk and Eli Lilly. EB has received research funding from the Juvenile Diabetes Research Foundation and Dexcom and receipt of study devices from Dexcom. YCK reports grants from the Helmsley Foundation and NIH (1R01DK120358–0), product support from Dexcom, and is serving as site Principal Investigator on grants from Medtronic Diabetes, Tandem Diabetes, and Dexcom. ERM received research grants from Novo Nordisk for a randomised controlled trial investigating the use of faster aspart in comparison with aspart in pregnant women with pre-existing diabetes, a study evaluating the effect of insulin pump treatment in an international prospective cohort, and for the EXPECT study on the effect of insulin Degludec in comparison with insulin detemir in pregnant women with type 1 diabetes. In addition, ERM received funding from Novo Nordisk for lectures on diabetes in pregnancy and for attending the European Association for the Study of Diabetes Annual Meeting 2022. TB has received honoraria for participation on advisory boards for Novo Nordisk, Sanofi, Eli Lilly, Medtronic, Provention Bio, and Indigo Diabetes, and as a speaker for Astra Zeneca, Eli Lilly, Novo Nordisk, Medtronic, Abbott, Dexcom, Sanofi, and Roche. TB's institution, University Medical Centre Ljubljana, has received research grant support and travel expenses from Abbott, Medtronic, Novo Nordisk, Sanofi, Sandoz, Novartis, the EU, and the NIH–National Institute of Diabetes and Digestive and Kidney Diseases.

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