

Appendix

Table of contents

Table S1. Checklist for healthcare providers relevant to pregnancy care in the comprehensive, preconception-to-pregnancy management plan.	2
Table S2. One-page educational leaflet for women with type 1 diabetes and their families.	3
Table S3. List of management centres that provided the comprehensive, preconception-to-pregnancy management plan.	4
Data collection	5
Management of Care Integration	7
Table S4. List of comparison centres.	8
Table S5. Definition of pregnancy outcomes.....	9
Table S6. Causes of miscarriage in the second trimester and stillbirth in the participants.	10
Table S7. Logistic regression analyses of the association of the comprehensive management plan with adverse pregnancy outcomes in the studied women with type 1 diabetes.	11
Table S8. Comparison of the rate of severe adverse pregnancy outcome in the study population receiving or missing preconception care.....	12
Table S9. Glycemic control and pregnancy outcomes among pregnant women with type 1 diabetes who used continuous glucose monitoring during pregnancy and those who did not in the prospective cohort.	13

Table S1. Checklist for healthcare providers relevant to pregnancy care in the comprehensive, preconception-to-pregnancy management plan.

Checklist Items	Check if done	Referral
PCC/1st trimester (<14 Weeks)		
1. Hand out the one-page educational leaflet for the woman with T1D and the family	<input type="checkbox"/>	
2. Folic acid supplementation	<input type="checkbox"/>	
3. Glucose monitoring 3.1 Performed ≥ 7 times of SMBG per day, OR use of CGM	<input type="checkbox"/>	
3.2 Target: premeal, bedtime, and overnight glucose 3.3 – 5.4 mmol/L; peak postprandial glucose 5.4 – 7.1 mmol/L	<input type="checkbox"/>	
4. Hypoglycemia prevention and treatment measures	<input type="checkbox"/> Yes <input type="checkbox"/> No	Endocrinology
5. Testing HbA1c every two months HbA1c > 10%	<input type="checkbox"/> Yes <input type="checkbox"/> No	(advises do not get pregnant during PCC phase) Endocrinology
6. Begins with intensive insulin therapy (MDI or CSII)	<input type="checkbox"/>	
7. Prevention of DKA	<input type="checkbox"/>	
8. Pregestational hypertension or DKD	<input type="checkbox"/> Yes <input type="checkbox"/> No	Endocrinology
9. Discontinuation of teratogenic drugs	<input type="checkbox"/>	
10. Screening for: uACR ≥ 30 mg/mmol (0.3 mg/mg), or ≥ 300 mg/day; or urine test paper ≥ 1 g/L (“2+”); or serum creatinine level elevated*	<input type="checkbox"/> Yes <input type="checkbox"/> No	Endocrinology
11. Screening thyroid function	<input type="checkbox"/>	
2nd and 3rd trimester		
Repeat items 3–11 above	<input type="checkbox"/>	
12. Weight gain during pregnancy is not within the curve [#]	<input type="checkbox"/>	Nutritionist / Endocrinology
13. Testing HbA1c every two months (target: < 6.5%) HbA1c > 7.5%	<input type="checkbox"/> Yes <input type="checkbox"/> No	Endocrinology
14. The 24-hour urinary protein quantitative ≥ 300 mg/dl, or uACR ≥ 0.3 mg /mmol, or protein \geq “2+” in urinary routine examination	<input type="checkbox"/> Yes <input type="checkbox"/> No	Obstetric high-risk pregnancy clinic (advises low-dose aspirin.)
15. BP $\geq 140/90$ mmHg	<input type="checkbox"/>	Obstetric high-risk pregnancy clinic
Delivery and breastmilk		
16. Monitors BG hourly at the beginning of the 2 nd stage of labor	<input type="checkbox"/>	
17. Stop subcutaneous insulin, change to i.v. insulin	<input type="checkbox"/>	
18. Insulin regimen adjustment according BG, keep BG level at 3.9 – 5.6 mmol/L	<input type="checkbox"/>	
19. BG test of newborn at 15min, 30min, 1h, 12h, 24h, 48h after birth	<input type="checkbox"/>	
20. Prevention of hypoglycemia during lactation	<input type="checkbox"/>	

This checklist was inserted to the universal antenatal record, which is part of the preexisting Chinese nationwide universal maternal care framework following the World Health Organization guidance. *According to the reference range where the test was performed.

Abbreviations: PCC, preconception care; T1D, type 1 diabetes; SMBG: Self-monitoring of blood glucose; CGM, continuous glucose monitoring; HbA1c, haemoglobin A1c; MDI: multiple daily injections of insulin; CSII: continuous subcutaneous insulin injection; DKD: diabetes kidney disease; DKA: diabetic ketoacidosis; uACR: Urinary albumin /creatinine ratio; BG: blood glucose; i.v., intravenous.

Table S2. One-page educational leaflet for women with type 1 diabetes and their families.

- **Glycemic target during pregnancy:**
 - **Haemoglobin A1c (HbA1c) < 6.5%**
 - Premeal, bedtime, and overnight fingertip glucose **3.3 – 5.4 mmol/L**;
 - Peak postprandial fingertip glucose **5.4 – 7.1 mmol/L**.
- Please **DO** carbohydrate counting.
- Reasonable choice of exercise, light and moderate aerobic exercise.
- Diabetes is not an indication of cesarean section.
- Diabetes and insulin therapy are not contraindications for breastfeeding.
- Prevent hypoglycemia during lactation.

Warning signs	Please go to visit
<ul style="list-style-type: none"> ● Have feelings like chest tightness, shortness of breath, and reduced urine volume; ● Conditions existing before pregnancy, such as vascular lesions or hypertension. 	Obstetric high-risk pregnancy clinic
<ul style="list-style-type: none"> ● Conditions existing before pregnancy that requires medication 	Endocrinology
<ul style="list-style-type: none"> ● Two consecutive blood pressures more than four hours apart $\geq 140 / 90$ mmHg 	Obstetric high-risk pregnancy clinic
<ul style="list-style-type: none"> ● Diagnosed diabetes before 10-year old; Or having diabetes > 10 years; Or have diabetes kidney disease 	Obstetric high-risk pregnancy clinic / Endocrinology
<ul style="list-style-type: none"> ● HbA1c > 10% before getting pregnant; Or > 7.5% during pregnancy 	Endocrinology
<ul style="list-style-type: none"> ● Three consecutive times out of glycemic target range within a week 	Endocrinology
<ul style="list-style-type: none"> ● Frequent occurrence of hypoglycemia or severe hypoglycemic episodes 	Endocrinology

Please scan the QR code on the left to access the free online courses on type 1 diabetes, planning pregnancy and pregnancy with diabetes. Online peer support is also available.



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Table S3. List of management centres that provided the comprehensive, preconception-to-pregnancy management plan.

1.	The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou
2.	Peking University First Hospital, Beijing
3.	Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai
4.	West China Hospital, Chengdu
5.	Peking Union Medical College Hospital, Beijing
6.	Nanjing Drum Tower Hospital, Nanjing
7.	The Second Affiliated Hospital of Suzhou University, Suzhou
8.	The Second Xiangya Hospital of Central university, Changsha
9.	Jiangsu Province Hospital, Nanjing
10.	Shandong Provincial Hospital, Jinan
11.	Changhai Hospital, Shanghai

Data collection

The prospective cohorts

We prospectively collected data from the pregnant women with T1D in the prospective cohort who received the comprehensive preconception-to-pregnancy management plan at the management centres between January 1, 2014 and December 31, 2017.

The diagnosis of T1D was a clinical diagnosis which was based on the American Diabetes Association descriptions of type 1 diabetes (American Diabetes Association, 2013, *Diabetes Care*,) and the World Health Organization reports on the classification of diabetes (Alberti KG and colleagues, 1998, *Diabetic Medicine*). The data sources were (1) the participants' universal antenatal care records (pregnancy notes), (2) the checklist for relevant healthcare providers (HCPs) that was inserted to their pregnancy notes, and (3) their in-patient medical record during their peri-pregnancy period. First, the pregnancy handhold notes is part of the preexisting nationwide universal maternal care pathway based on the World Health Organization's guidance. Every pregnant woman in China receives an individual antenatal care record book (pregnancy handhold notes) at their first antenatal visit once pregnancy has been confirmed. The pregnancy notes documents information of the visits of the universal maternal care pathway (see Figure 1, the block on the right), briefly the maternal anthropometry, laboratory and other test results, and fetal/neonatal/infant details, from preconception to postpartum. Second, the checklist for the HCPs is part of the comprehensive, evidence-based preconception-to-pregnancy management plan for T1D that was implemented in the management centres. The checklist was inserted to the pregnancy notes of the pregnant women with T1D. In this checklist, additional information, such as extra clinic visits, results of extra haemoglobin A1c measurements and urinary albumin to creatinine ratio would be recorded. Third, we also used the in-patient medical records at the management centre of the participants as a source for information of any hospitalization during pregnancy, including delivery. From these medical records, we obtained information on maternal and neonatal pregnancy outcomes, delivery information and infant birth details, newborn assessment details and infant morbidity details.

Data of the universal antenatal records and the checklists of the women in the prospective cohort were collected at their last visit (42 days postpartum) at the management centres. All clinical data were obtained from chart review of these archived pregnancy notes. Data were also extracted from the in-patient medical records of the participants from the medical department of the management centres.

The comparison populations

Medical records of eligible participants were retrieved from the hospital information system based on ICD code by the staff of the medical record department of the management centres and the comparison centres. The medical records were anonymized and reviewed by a trained investigator of the study group. Briefly, the following information was extracted:

- Maternal data: preconception and during pregnancy
 - Anthropometry
 - Demographic and social characteristics
 - History of tobacco and alcohol intake
 - Diabetes related medical history

- Other medical and obstetric histories
- Maternal and neonatal pregnancy outcomes
- Delivery information and infant birth details
- Newborn assessment details
- Infant morbidity details

Management of Care Integration

Here we briefly introduce the management of care integration. When there was an indication of integration, as the management plan (Figure 1), the checklist (Appendix, Table S1) or the education leaflet (Appendix, Table S2) suggested, or depending on the doctor's judgement, the endocrinology team was involved. The endocrinology team looking after the woman's diabetic control would write in the pregnancy handhold notes or in the checklist that would be accessible to both the woman and her obstetric team. If there was a need for the endocrinology and obstetric team to jointly discuss the woman's ongoing care, a multidisciplinary team would be confined. The multidisciplinary team would include endocrinologists, gynecologists/obstetricians, and relevant specialists (usually nephrologists, ophthalmologists and cardiologists). When necessary, hospital admission to either the endocrinology or gynecology/obstetrics ward would be arranged, and her clinical management discussed between the endocrinology and obstetric teams and documented in both the hospital and the woman's handhold pregnancy notes.

Table S4. List of comparison centres.

1.	The First Affiliated Hospital of Harbin Medical University, Harbin
2.	Shenzhen Second People's Hospital, the First Affiliated Hospital of Shenzhen University, Shenzhen
3.	First Affiliated Hospital of Zhengzhou University, Zhengzhou
4.	Women's Hospital, Zhejiang University School of Medicine, Hangzhou
5.	The First Affiliation Hospital of University of Science and Technology (Anhui Provincial Hospital), Hefei
6.	Shenzhen People's Hospital, the Second Clinical Medical College of Jinan University, Shenzhen
7.	School of medicine, Nanchang University, Nanchang
8.	Shenzhen Maternity and Child Healthcare Hospital Affiliated to Southern Medical University, Shenzhen
9.	The First Affiliated Hospital of Anhui Medical University, Hefei
10.	The Second Affiliated Hospital of Anhui Medical University, Hefei
11.	Xiangya Hospital of Central South University, Changsha

Table S5. Definition of pregnancy outcomes.

	Outcome	Definition
Maternal outcomes	Maternal mortality	Maternal mortality was defined as the death of a woman while pregnant within 42 days of termination of pregnancy, irrespective of the cause of death.
	Caesarean section	Extraction of the fetus(es) through an abdominal incision
	Pre-eclampsia	<i>de novo</i> hypertension after 20 th gestational week and the coexistence of one or more of the following new onset conditions: <ol style="list-style-type: none"> 1. Proteinuria (spot urine protein/creatinine ratio ≥ 30 mg/mmol (0.3 mg/mg) or ≥ 300 mg/day or at least 1 g/L ('2+') on dipstick testing) 2. Other maternal organ dysfunction: <ul style="list-style-type: none"> • Renal insufficiency (creatinine ≥ 0.09 μmol/L; 1.02 mg/dL) • Liver involvement (elevated transaminases: at least twice upper limit of normal and right upper quadrant or epigastric abdominal pain) • Neurological complications (examples include eclampsia, altered mental status, blindness, stroke, or more commonly hyperreflexia when accompanied by clonus, severe headaches when accompanied by hyperreflexia, persistent visual scotomata) • Hematological complications (thrombocytopenia: platelet count below 150,000/dL, disseminated intravascular coagulation, hemolysis) 3. Uteroplacental dysfunction Fetal growth restriction
	Miscarriage	Spontaneous loss of a pregnancy before the 20 th week of gestation.
	Stillbirth	Delivery of a fetus showing no signs of life as indicated by the absence of breathing, heartbeats, pulsation of the umbilical cord, or definite movements of voluntary muscles at 20 weeks or greater of gestation.
Neonatal outcomes	Congenital malformation(s)	Malformations that include ICD 10 codes: Q00–Q99.
	Hyperbilirubinemia	Need for phototherapy or exchange transfusion
	Respiratory distress syndrome	Respiratory difficulties requiring any positive pressure ventilation ≥ 24 hours that occur beyond the first 10 minutes of the resuscitation period, and/or given surfactant within 72 hours after birth.
	Admission to the neonatal intensive care unit	Admission to higher-level neonatal care unit or special care nursery for >24 hours during the initial hospitalization after birth
	Neonatal hypoglycemia	Neonatal hypoglycemia defined as a plasma glucose value below 2.2 mmol/L.
	Small-for-gestational age	defined as a birth weight below the 10 th percentile based on Chinese neonatal sex-specific birth weight charts for different gestational age (Zhu L and colleagues, 2015, Zhonghua Er Ke Za Zhi)
	Large-for-gestational age	defined as a birth weight above 90 th percentile based on Chinese neonatal sex-specific birth weight charts for different gestational age (Zhu L and colleagues, 2015, Zhonghua Er Ke Za Zhi)
	Macrosomia	Defined as birth weight $\geq 4,000$ grams irrespective of gestational age.

Table S6. Causes of miscarriage in the second trimester and stillbirth in the participants.

Time at miscarriage and stillbirth	Prospective cohort 2015 – 2017		Retrospective cohort 2012 – 2014		Comparison cohort 2015 – 2017	
	no.	Cause	no.	Cause	no.	Cause
13 th – 27 th gestational week	1	Miscarriage due to antiphospholipid antibodies syndrome	1	Gestational hypertension	1	Gestational hypertension
			2	Fetal major malformation		
			4	Intrauterine fetal death	1	Fetal major malformation
	1	Fetal heart malformation	1	Progress of diabetic kidney disease	5	Intrauterine fetal death
			2	Diabetic ketoacidosis	2	Spontaneous miscarriage
			1	Hyperemesis gravidarum	2	Unknown
28 th – 36 th gestational week	0	n/a	2	Intrauterine fetal death	2	Gestational hypertension
			2	Progress of diabetic kidney disease	5	Intrauterine fetal death
					2	Fetal major malformation
					2	Progress of diabetic kidney disease
					2	Unknown
Total	2		15		24	

Table S7. Logistic regression analyses of the association of the comprehensive management plan with adverse pregnancy outcomes in the studied women with type 1 diabetes.

	Unadjusted model		Multivariable model [#]	
	Odds ratio (95% CI) of management	<i>P</i> value	Odds ratio (95% CI) of management	<i>P</i> value
The prospective cohort (2015 – 2017) vs the comparison cohort (2015 – 2017)				
Severe adverse pregnancy outcome*	0.19(0.08 – 0.44)	<0.001	0.22(0.09 – 0.52)	0.001
Miscarriage in 2nd trimester and stillbirth	0.06(0.01 – 0.25)	<0.001	0.07(0.02 – 0.32)	0.001
Congenital malformation (s)	1.01(0.28 – 3.70)	0.985	0.91(0.24 – 3.48)	0.894
Admission to NICU	0.51(0.29 – 0.89)	0.018	0.38(0.20 – 0.71)	0.002
The prospective cohort (2015 – 2017) vs the retrospective cohort (2012 – 2014)				
Severe adverse pregnancy outcome*	0.23(0.13 – 0.65)	0.003	0.31 (0.13 – 0.74)	0.009
Miscarriage in 2 nd trimester and stillbirth	0.14(0.03 – 0.63)	0.010	0.15(0.03 – 0.74)	0.020
Congenital malformation(s)	0.52(0.19 – 1.46)	0.216	0.51(0.18 – 1.51)	0.226
Admission to NICU	0.56(0.33 – 0.93)	0.026	0.56(0.32 – 0.97)	0.039

In all the models, we included whether the subjects had access to the comprehensive management plan as an independent variable. The women in the prospective cohort had access to the comprehensive management plan, while those in the other two cohorts did not. *Severe adverse pregnancy outcome is a composite of maternal mortality, neonatal death, congenital malformation(s) and miscarriage in the second trimester and stillbirth. [#]In the multivariable models, we adjusted for age at conception, duration of diabetes at conception, pre-conceptional diabetic complication(s), and level of education.

Abbreviations: CI, confidential interval; NICU, neonatal intensive care unit.

Table S8. Comparison of the rate of severe adverse pregnancy outcome in the study population receiving or missing preconception care.

Rate (n/N) of severe adverse pregnancy outcome			
Receiving preconception care*	Prospective cohort 2015 – 2017	Retrospective cohort 2012 – 2014	Comparison cohort 2015 – 2017
Yes	5.69% (7/123)	38.71% (12/31)	25.86% (15/58)
No	10.00% (1/10)	49.18% (60/122)	24.14% (14/58)
<i>P</i> value Receiving vs. missing	0.582	0.297	0.830

*Receiving preconception care was defined as testing HbA1c during the preconception period or the first trimester of pregnancy.

Table S9. Glycemic control and pregnancy outcomes among pregnant women with type 1 diabetes who used continuous glucose monitoring during pregnancy and those who did not in the prospective cohort.

	Ever Used CGM during pregnancy	Not Using CGM during pregnancy	P value
No. of pregnant women	103	30	
Severe adverse pregnancy outcome*, n (%)	36(35.0)	7(23.3)	0.329
Maternal death, n (%)	0	0	NA
Caesarean section, n (%)	60(60.6)	21(72.4)	0.245
Pre-eclampsia, n (%)	5(4.8)	2(6.7)	0.716
Miscarriage in the 2 nd trimester and stillbirth, n (%)	1(1.0)	1(3.3)	0.288
Preconception body weight, Kg, mean±SD	54.36±7.76	57.15±8.33	0.148
Body weight at delivery, Kg, , mean±SD	67.64±7.63	68.19±8.13	0.894
Body weight gain, Kg, mean±SD	12.53±5.04	11.03±5.32	0.223
HbA1c at delivery,	–	–	–
%, mean±SD	6.10±0.76	6.16±0.74	0.734
Mmol/mol, mean±SD	43±8	44±8	0.734
n/N(%)	79/103(76.7)	7/30(23.3)	0.633
HbA1c ≤ 6.5% or 48 mmol/mol, n/N(%)	63/79(79.7)	5/7(71.4)	1.000
No. of live births	101	29	
Neonatal death, n (%)	0	0	NA
Congenital malformation, n (%)	5(5.9)	0(0.0)	0.337
LGA, n (%)	12(11.9)	7(24.1)	0.137
Neonatal hypoglycemia, n (%)	16(15.8)	4(13.8)	1.000
Admission to NICU, n (%)	31(30.7)	6(20.7)	0.356

*Severe adverse pregnancy outcome comprised of maternal death; neonatal death; neonatal malformation; and miscarriage in the 2nd trimester and stillbirth.