Supplemental Online Content

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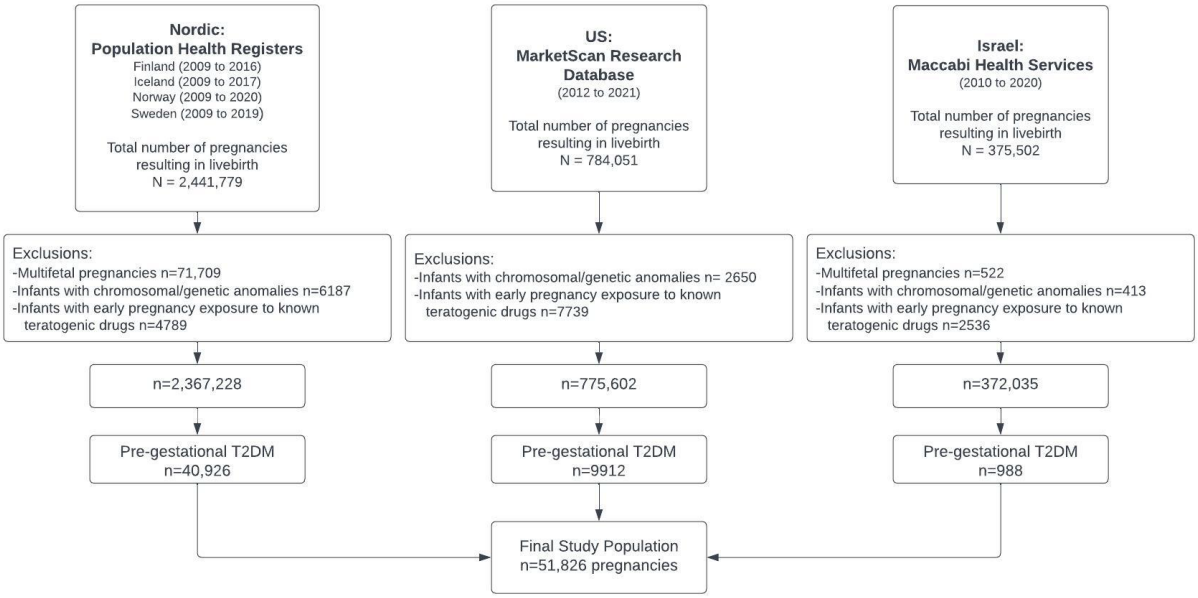
This supplemental material has been provided by the authors to give readers additional information about their work.

Supplementary Figure 1: Flow chart outlining the derivation of the study population



Abbreviations: T2DM, type 2 diabetes mellitus

Supplementary Table 1. Known Teratogenic drugs

Drug	US MarketScan (identified by generic drug names)	Nordic cohort and Israel-MHS (ATC Codes)
Warfarin	Yes	B01AA03
Antineoplastic drugs:	Yes	L01DA L01AB01 L01AA02 M04AC01 L01AA01 L01DB01 L01BB02 L01BA01, L04AX03 L01CA01 L01CA02
Lithium	yes	N05AN01
Topical or systemic retinoids, including isotretinoin	yes	D10BA01 D10AD54 D10BA04 D05BB D11AH04
Misoprostol	yes	A02BB01, G02AD06 M01AE56 M01AB55
Thalidomide	yes	L04AX02
Valproic acid	yes	N03AG01
Carbamazepine	yes	Nordics: not included[a] Israel: N03AF01

[a] based on recent evidence of no teratogenic effect of carbamazepine in Nordic populations(1)

Supplementary Table 2. Antidiabetic Medications

Antidiabetic Medication Class	US MarketScan Research Database (Generic names)	Nordic cohort and Israel-MHS (ATC Codes)
Insulin	Insulin Aspart Protamine/ Insulin Aspart Insulin Aspart, Recombinant Insulin Aspart/ Insulin Aspart Protamine Insulin Degludec Insulin Degludec/Liraglutide Insulin Detemir Insuline Glargine, Recombinant Insulin Glargine, Recombinant/Lixisenatide Insulin Glulisine Insulin Human Inhaled Insulin Human Isophane Insulin Human Isophane/ Insulan Human Regular Insulin Human Regular Insulin Human Zinc (LEnte) Insulin Lispro Protamine/ Insulin Lispro Insulin Lispro, Recombinant Insulin Lispro/ Insulin Lispro Protamine	A10A
Metformin (only)	Metformin Hydrochloride	A10BA02
Sulfonylureas	Chlorpropamide Glimepiride Glimepiride/Pioglitazone Hydrochloride Glipizide Glipizide/Metformin Hydrochloride Glyburide Glyburide, Micronized Glyburide/Metformin Hydrochloride Tolazamide Tolbutamide Acetohexamide	A10BB A10BD01 A10BD02 A10BD04 A10BD06
Dipeptidyl peptidase 4 inhibitors	Alogliptin Benzoate Alogliptin Benzoate/Metformin Hydrochloride Alogliptin Benzoate/Pioglitazone HCl Empagliflozin/Linagliptin Linagliptin Linagliptin/Metformin Hydrochloride Metformin Hydrochloride/Saxagliptin Hydrochloride Metformin Hydrochloride/Sitagliptin Phosphate Saxagliptin Hydrochloride Simvastatin/Sitagliptin Phosphate Dapagliflozin/Saxagliptin Sitagliptin Phosphate	A10BH A10BD07 A10BD08 A10BD09 A10BD10 A10BD11 A10BD12 A10BD13 A10BD18 A10BD19 A10BD21 A10BD24 A10BD25 A10BD27
Glucagon-like peptide-1 receptor agnists	Albiglutide Dulaglutide Exenatide Liraglutide Insulin Degludec/Liraglutide Lixisenatide Insulin Glargine, Recombinant/Lixisenatide Semaglutide	A10BJ
Sodium-glucose co-transporter 2 inhibitors	Canagliflozin Canagliflozin/Metformin Hydrochloride Dapagliflozin Dapagliflozin/Metformin Hydrochloride Dapagliflozin Propanediol Dapagliflozin Propanediol/Metformin Hydrochloride Dapagliflozin/Saxagliptin Empagliflozin Empagliflozin/Linagliptin Empagliflozin/Metformin Hydrochloride Ertugliflozin	A10BK A10BD15 A10BD16 A10BD19 A10BD20 A10BD21 A10BD22 A10BD23 A10BD24 A10BD25 A10BD27

Other antidiabetic medication (Alpha glucosidase inhibitors, thiazolidinediones, meglitinides)	Acarbose Miglitol Glimepiride/Pioglitazone Hydrochloride Metformin Hydrochloride/Pioglitazone Hydrochloride Metformin Hydrochloride/Rosiglitazone Maleate Alogliptin Benzoate/Pioglitazone HCl Pioglitazone Hydrochloride Rosiglitazone Maleate Metformin Hydrochloridel/Rosiglitazone Maleat Troglitazone Pramlintide Acetate Nateglinide Repaglinide	A10BF A10BD17 A10BG A10BD03 A10BD04 A10BD05 A10BD06 A10BD09 A10BD12 A10BD26 A10BX A10BD14

Supplementary Table 3. Definition of Major Congenital Malformations of Interest in Nordic Countries

Outcomes are defined based on data from the Medical Birth, Malformation and/or Patient Registers from the date of birth to one year after birth.
For diagnoses recorded in the inpatient setting, one code was considered sufficient.
For diagnoses recorded in the outpatient setting, at least 2 codes recorded on different days were required.

Note: While malformation subgroups 1-3 and 5-12 were not considered as separate outcomes in the analyses, we present the definition of these subgroups as they are used to define major congenital malformations overall.

Subgroup	ICD-10	ICD-9A (Finland)[a]
1. Nervous system	Q00-Q07 Except (Q04.61, Q07.80, Q07.82)	740-742 Except 74280
2. Eye	Q10-Q15 Except Q10.1-Q10.3, Q10.5, Q13.5	743 Except 74345, 74361-74363, 74365
3. Ear, face, and neck	Q16-Q18 Except Q17.0-Q17.5, Q17.9, Q18.0-Q18.2, Q18.4-Q18.7, (Q18.80), Q18.9	744 Except 7441, 74420-74424, 74430, 7444, 74480-74483, 7449
4. Cardiac	Q20-Q26 Except (Q21.11), Q246, Q250 and preterm, (Q25.41), Q25.6 and preterm, Q26.1	745, 746, 7470-7474 Except 74550, 74687, 7470 and preterm, 74723, 747325 and preterm, 74741, 74749
5. Respiratory	Q30, Q32-Q34 Except Q30.1-Q30.9, Q32.0, Q32.2, (Q33.00), Q33.1, Q33.6	748 Except 7481, 7482-7483 (other), 74840, 74851, 74859, 74862
6. Oro-facial clefts	Q35-Q37 Except Q35.7, or if occurring with Q00, Q042	749 Except 74908, or if occurring with 740, 74226
7. Digestive system	Q38-Q45, Q79.0 Except Q38.1, Q38.2, (Q385.0), Q40.0, Q40.1, (Q40.21), Q43.0, (Q43.20, Q43.81, Q43.82), Q44.4, (Q458.3)	750, 751, 7566 Except 75000, 75011-75013, 75024, 75050, 75051, 7506, 75101, 7513, 75166
8. Abdominal wall	Q79.2, Q79.3, Q79.5	75670, 75671, 75679
9. Genital	Q50-Q56 Except Q50.1 (Q50.10, Q50.11), Q50.2, Q50.5, Q52.3, Q52.5, Q52.7, Q53, Q54.4, (Q55.20, Q55.21)	752 Except 75208, 75211, 75243, 75244, 7525, 75261 (urinary), 752621, 75282, 75286
10. Urinary	Q60-Q64, Q79.4 Except Q61.0, (Q61.90 genetic) Q62.7, Q63.3	75261, 753, 75672 Except 75310, 75334, 753485
11. Limb[b]	Q66-Q74 Except Q66.1-Q66.9, Q67.0-Q67.8, Q68.0, (Q68.10, Q68.21) Q68.3, Q68.4, Q68.5, (Q74.00)	754-755 Except 7540-7542 (other), 7543, 75440-75443, 75451-75453, 75459, 7546, 7547, 75480-75482, 755525, 755606, 755616, 755645, 755646, 75566, 75581 (genetic)
12. Other	Q27, Q28, Q31, Q75-Q85, Q89 Except Q27.0, Q31.4, Q75.1 (genetic), Q75.2, Q75.3, Q75.4 (genetic), Q76.0, (Q76.43, Q76.60, Q76.62), Q76.5, (Q76.71), Q79.0 (digestive), Q79.2 (abdominal wall), Q79.3 (abdominal wall), Q79.4 (urinary), Q79.5 (abdominal wall), Q82.5, Q82.8, Q83.3, Q84.5, Q84.6, (Q89.11), Q89.9	7475-7479, 7482-7483, 7540-7542, 756, 757, 759 Except 7475, 74836, 7540, 7541, 75421, 75604 (genetic), 756085, 75610, 7562, 75630, 75632, 75633, 7566 (digestive), 75670 (abdominal wall), 75671 (abdominal wall), 75672 (urinary), 75679 (abdominal wall), 75686, 7572, 7573, 75751, 75758, 75765, 75902, 75904, 75911, 7598 (genetic), 7599
X. Chromosomal anomaly, genetic syndrome, or teratogenic infection	D82.1, P35.0, P35.1, P37.1, (Q61.90), Q75.1, Q75.4, Q87, Q90-Q99 Except Q95	27911, 75581, 75604, 758, 7598, 7710, 7711, 77121 Except 7584, 75989
Any MCM[c]	**Any of the subgroups 1-12, excluding those in subgroup X**	

The definition of major congenital malformations was based on EUROCAT (EUROCAT [2013]. EUROCAT Guide 1.4: Instruction for the registration of congenital anomalies. EUROCAT Central Registry, University of Ulster. Version 01/12/2020). Codes in parentheses under ICD-10 are minor anomalies coded according to British Paediatric Association (BPA) modification of ICD that cannot be identified with standard ICD-10. The Finnish Register of Congenital Anomalies uses ICD-9A (A=Atlanta or Metropolitan Atlanta Congenital Defects Program [MACDP] which is almost identical to BPA version). [a]It is possible to exclude more minor anomalies with ICD-9A than standard ICD. [b]Due to concerns of low validity, we did not include hip dislocation or dysplasia (ICD-10 Q65; ICD-9A 7543, 75566). [c]Due to concern that we may exclude children exposed to potentially teratogenic medications of interest ICD-10 code Q86 (congenital malformation syndromes due to known exogenous causes, not elsewhere classified) and ICD-9A code 75989 were neither excluded nor included in any subgroup.

Supplementary Table 4. Definition of Major Congenital Malformations of Interest in MarketScan Research Database and Maccabi Health Services Database

The approach described here has previously been validated to identify several of the described malformations of interest in another US health care database with high positive predictive values.(2, 3)

MarketScan Research Database: Consider claims in infant record between date of birth (DOB) and DOB+90 and/or in the maternal record between delivery and delivery+30, using both in- and out-patient data. Refer to the ICD-9 codes in eTable 2 below.

Maccabi Health Services (MHS) Database: Consider claims in infant records between DOB and DOB+1 year.

For cardiovascular malformations overall:
The outcome is considered present if there are

- ≥ 2 dates with a code for any of the cardiac malformations (regardless of the subgroup) OR
- ≥ 1 date with a code for any of the cardiac malformations* and a cardiac procedure code OR (no produre codes for MHS)
- ≥ 1 date with a code for any of the cardiac malformations* and the infant died within the first 90 days (1 year for MHS).

The outcome is considered maternal if there is ≥1 date with a code of interest in the maternal records between LMP and LMP+105 AND there are no codes in the infant record between DOB and DOB+90.

For non-cardiovascular malformations and malformation subgroups:
The outcome is considered present if there are

- ≥ 2 dates with a code for the malformation group/subgroup OR
- ≥ 1 date with a code for the malformation group/subgroup and an outcome-specific procedure code OR
- ≥ 1 date with a code for the malformation group/subgroup and the infant died within the first 90 days (1 year for MHS).

The outcome is considered maternal if there is ≥1 date with a code of interest in the maternal records between LMP and LMP+105 AND there are no codes in the infant record between DOB and DOB+90.

For any major congenital malformation:
The outcome is considered present if the infant contributed either to any of the non-cardiovascular malformations or to cardiovascular malformations overall.

*the following codes should not be considered: 745.4x, 745.5x, 747.0x, 746.4x, 746.6x, 746.99, 747.3x if preterm, 746.02 if preterm, 747.5x, 416.0x if preterm, 747.83 if preterm, 746.08, 746.105

MALFORMATION GROUP	Malformation Subgroup	ICD-9	ICD-10
1. Cardiovascular Anomalies	Conotruncal Defects	745.0x, 745.1x, 745.2x	Q20.0-Q20.3, Q20.5, Q20.8, Q21.3
	Single Ventricle	745.3x	Q20.4
	Ventricular Septal Defect**	745.4x	Q21.0
	ASD	745.5x AND no preterm[2]	Q21.1 AND no preterm[2]
	AV Septal Defect	745.6x	Q21.2
	Right sided defects	746.00, 746.01, 746.09, 746.1x, 746.2x, 746.83, 747.3x AND no preterm[2], 746.02 AND no preterm[2]	Q22, Q22.0, Q22.1 AND no preterm[2], Q22.3-Q22.9, Q24.3, Q25.5 AND no preterm[2], Q25.6 AND no preterm[2], Q25.7x AND no preterm[2]
	Left sided defects	747.1x, 747.2x, 746.3x, 746.5x, 746.7x, 746.81, 746.82	Q23, Q23.0, Q23.2, Q23.4, Q23.8, Q23.9, Q24.2, Q24.4, Q25.1x-Q25.4x
	PDA	747.0x and no preterm[2]	Q25.0 AND no preterm[2]
	PPHN	(416.0x or 747.83) and no preterm	(I27.0, P29.3x) AND no preterm
	Great cardiac veins	747.4 747.41 747.42	Q26.0-Q26.4
	Other cardiac	745.7x,745.8x, 746.8[1], 746.84-746.89	Q20.6, Q21.4, Q21.8, Q24.0, Q24.1, Q24.5, Q24.6, Q24.8, Q25.8
	Cardiac NOS	745[1], 745.9, 746[1], 746.9x (do not count 746.99), 747[1]	Q20[1], Q20.9, Q21[1], Q21.9, Q24[1], Q24.9, Q25[1], Q25.9≥
2. Oral cleft		749.xx	Q35.x-Q37.x
3. Central Nervous System		740.xx-742.xx	Q00.x-Q07.x
4. Eye Anomalies		743.xx (do not count 743.6x, 743.8x)	Q10[1], Q10.4, Q10.7, Q11.x-Q15.x (do not count Q13.5)
5. Ear Anomalies		744.0x, 744.23, 744.3x	Q16.x-Q17.x (do not count Q17.0, Q17.3, Q17.5)
6. Other vascular (non-cardiac)		747.40, 747.49, 747.6x-747.9x (do not count 747.83)	Q26.5-Q26.9, Q27.x-Q28.x (do not count Q27.0, Q27.4)

7. Respiratory malformations		748.xx (do not count 748.1x, 748.3x)	Q30.0, Q30.1, Q31.0, Q32.x (do not count Q32.0), Q33.x (do not count Q33.1), Q34.x
8. Gastrointestinal		750.xx-751.xx (do not count 750.0x, 750.1x, 751.0x)	Q38.x-Q45.x (do not count Q38.1, Q38.2, Q38.3, Q43.0)
9. Genital (male and female)	Overall	752.xx (do not count 752.42, 752.52) (in addition, do not count 752.5x if preterm), 756.71	Q50.xx-Q52.xx (do not count Q52.3, Q52.5), Q53.0x, Q53.1xx AND no preterm, Q53.2xx AND no preterm, Q53.9 AND no preterm, Q54.xx-Q56.xx (do not count Q55.22), Q64.0, Q79.4
	Hypospadias	752.61	Q54.x (do not count Q54.4)
	Cryptorchidism	752.5x (do not count 752.52) (in addition, do not count 752.5x if preterm)	Q53.xxx AND no preterm
10. Urinary		753.xx (do not count 753.7x), 756.71	Q60.xx-Q64.xx (do not count Q64.0, Q64.4), Q79.4
11. Musculoskeletal		754.1x, 754.2x, 756.xx (do not count 756.2x, 756.7x)	Q68.0, Q75.x-Q78.x (do not count Q76.5), Q79.0, Q79.1, Q79.6, Q79.8, Q79.9
12. Limb defects (includes hip)		755.xx (do not count 755.65, 755.63), 754.4x-754.8x (do not count 754.81, 754.82)	Q65.81, Q65.82, Q66.xx, Q68.1-Q68.8, Q69.x-Q74.x
13. Abdominal Wall		756.7x	Q79.2- Q79.5x
14. Other		757.0x, 757.1x, 759.xx (do not count 759.5x, 759.81-759.83)	Q80.8, Q80.9, Q86.x, Q89.xx

[1] Only count this code. Do not count any digits after this code.
[2] In order for this malformation to be present, ≥ 2 dates with a diagnostic code for a malformation of which at least one code is documented at >= 6 weeks after DoB are required.

The 13 groups numbered above present the main classes of malformation. An infant with one of these confirmed malformations (specific inclusion criteria see above) would be considered to have a major malformation, acknowledging that the "other" malformations may include a range of defects and the specificity might not be as high as for others. However, these groups should be relatively small.

A separate group are infants with **chromosomal anomalies and excluded from the study population**. Defined as:

- ≥ 2 dates with a code for a malformation within the group "chromosomal abnormalities"
- 1 date with a code for a malformation within the group and infant death

Chromosomal abnormalities	Dx	ICD9: 758xx, 75981, 75982, 75983	ICD-10: Q87.1, Q87.11 Q87.19 Q87.40, Q87.410, Q87.418, Q87.42, Q87.43, Q90.0, Q90.1, Q90.2, Q90.9, Q91.0, Q91.1, Q91.2, Q91.3, Q91.4, Q91.5, Q91.6, Q91.7, Q92.0, Q921, Q92.2, Q92.5, Q92.61, Q92.62, Q92.7, Q92.8, Q92.9, Q93.0, Q93.1, Q93.2, Q93.3, Q93.4, Q93.5, Q93.7, Q93.81, Q93.88, Q93.89, Q93.9, Q95.0, Q95.1, Q95.2, Q95.3, Q95.5, Q95.8, Q95.9, Q96.0, Q96.1, Q96.2, Q96.3, Q96.4, Q968, Q96.9, Q97.0, Q97.1, Q97.2, Q97.3, Q97.8, Q979, Q980, Q98.1, Q98.3, Q98.4, Q98.5, Q98.6, Q98.7, Q98.8, Q98.9, Q99.0, Q99.1, Q99.2, Q99.8, Q99.9

Supplementary Table 5. Definition and Assessment Period of Covariates of Interest

Condition	US (MarketScan Research Database)	Nordic Registers	Israel (Maccabi Health Services Database)
Demographic characteristics			
Year of infant birth	yes	As recorded in birth register	As recorded in the electronic medical record
Maternal age at infant birth	yes	As recorded in birth register	As recorded in the electronic medical record
Country of infant birth	n/a	Finland, Iceland, Norway, Sweden	Israel
Maternal conditions	≥1 inpatient or outpatient code in maternal record from LMP-180 to LMP+90	As recorded in patient register or birth register from LMP-365 to LMP+97	Assessment period = LMP-180 to LMP+90
Obesity or overweight	**ICD-9:** 278.0x, 649.1x, V85.3x, V85.4x **ICD-10:** E66.01, E66.09, E66.1, E66.2, E66.3, E66.8, E66.9, O99.210, O99.211, O99.212, O99.213, O99.214, O99.215, Z68.30, Z68.31, Z68.32, Z68.33, Z68.34, Z68.35, Z68.36, Z68.37, Z68.38, Z68.39, Z68.41, Z68.42, Z68.43, Z68.44, Z68.45	BMI≥30 as calculated from height and weight collected in early pregnancy. Available from 2012 for Iceland.	ICD-9: 278.0x or BMI>25 in LMP-365 to LMP+90
Chronic hypertension	**ICD-9:** 401.x-405.x, 642.0x-642.2x, 642.7x, 642.9x **ICD-10:** I1.0, I1.10, I1.19, I1.20, I12.9, I13.0, I13.10, I1.311, I13.2, I15.0, I15.1, I15.2, I15.8, I159, I16.0, I161, I16.9, O10.011, O10.012, O10.013, O10.019, O10.02, O10.03, O10.111, O10.112, O10.113, O10.119, O10.12, O10.13, O10.211, O10.212, O10.213, O10.219, O10.22, O10.23, O10.311, O10.312, O10.313, O10.319, O10.32, O10.33, O10.411, O10.412, O10.413, O10.419, O10.42, O10.43, O10.911, O10.912, O10.913, O10.919, O10.92, O10.93, O11.1, O11.2, O11.3, O11.4, O11.5, O11.9, O16.1, O16.2, O16.3, O16.4, O16.5, O16.9	**ICD-10:** O10, O16, I10-15	Meeting one the following: (1) ICD-9 codes 401.x-405.x; (2) At least 4 abnormal blood pressure measurements (systolic >140, diastolic>90), which account for at least 50% of all available measurements; (3) at least 6 dispensing records in a 3-year period for one of the following classes of medications: thiazides, calcium channel and beta blockers, ACE (angiotensin converting enzyme) inhibitors or ARBs (angiotensin-receptor blockers)
Diabetic complications	**ICD-9:** 583.81, 250.4x, 362.0x, 250.5x, 366.41, 365.44, 362.83, 707.1x, 585.3, 585.4, 585.5, 585.6, 582.xx, 583.xx, 585.1, 585.2, 585.9, 586.xx, 587.xx, 642.1x, 250.4x, 250.40, 250.41, 250.42, 250.43, 403.xx, 404.xx, 572.4x, 580.xx, 584.xx, 580.0x, 580.4x, 580.89, 580.9x, 582.4x, 642.1x, 791.2x, 791.3x **ICD-10:** E08.21, E08.40, E08.41, E08.42, E08.43, E09.21, E11.0, E11.1, E11.21, E11.22, E11.29, E11.31, E11.311, E11.319, E11.32, E11.321, E11.3211, E11.3212, E11.3213, E11.3219, E11.329, E11.3291, E11.3292, E11.3293, E11.3299, E11.33, E11.331, E11.3311, E11.3312, E11.3313, E11.3319, E11.339, E11.3391, E11.3392, E11.3393, E11.3399, E11.34, E11.341, E11.3411, E11.3412, E11.3413, E11.3419, E11.349, E11.3491, E11.3492, E11.3493, E11.3499, E11.35, E11.351, E11.3511, E11.3512, E11.3513, E11.3519, E11.352, E11.3521, E11.3522, E11.3523, E11.3529, E11.353, E11.3531, E11.3532, E11.3533, E11.3539, E11.354, E11.3541, E11.3542, E11.3543, E11.3549, E11.355, E11.3551, E11.3552, E11.3553, E11.3559, E11.359, E11.3591, E11.3592, E11.3593, E11.3599, E11.36, E11.37, E11.37X1, E11.37X2, E11.37X3, E11.37X9, E11.39, E11.40, E11.41, E11.42, E11.43, E11.44, E11.49, E11.610, E11.621, E11.7, E11.8, E13.21, E13.22, E13.29, E13.31, E13.311, E13.319, E13.32, E13.321, E13.3211, E13.3212, E13.3213, E13.3219, E13.329, E13.3291, E13.3292, E13.3293, E13.3299, E13.33, E13.331, E13.3311, E13.3312, E13.3313, E13.3319, E13.339, E13.3391, E13.3392, E13.3393, E13.3399, E13.34, E13.341, E13.3411, E13.3412, E13.3413, E13.3419, E13.349, E13.3491, E13.3492, E13.3493, E13.3499, E13.35, E13.351, E13.3511, E13.3512, E13.3513, E13.3519, E13.352, E13.3521, E13.3522, E13.3523, E13.3529, E13.353, E13.3531, E13.3532, E13.3533, E13.3539, E13.354, E13.3541, E13.3542, E13.3543, E13.3549, E13.355, E13.3551, E13.3552, E13.3553, E13.3559, E13.359, E13.3591, E13.3592, E13.3593, E13.3599, E13.36, E13.37, E13.37X1, E13.37X2, E13.37X3, E13.37X9, E13.39, E13.40, E13.41, E13.42, E13.43, E13.44, E13.49, E13.610, E13.621, G63.2, H28.0, H34.81, H34.811, H34.8110, H34.8111, H34.8112, H34.812, H34.8120, H34.8121, H34.8122, H34.813, H34.8130, H34.8131, H34.8132, H34.819, H34.8190, H34.8191, H34.8192, H34.83, H34.831, H34.8310, H34.8311, H34.8312, H34.832, H34.8320, H34.8321, H34.8322, H34.833, H34.8330, H34.8331, H34.8332, H34.839,	**ICD-10:** E11.0-E11.8, E16.0, H28.0, H36.0, G59.0, G63.2, G73.0, G99.0, I79.2, M14.2, M14.6, N08.3	**ICD-9:** 583.81, 250.4x, 362.0x, 250.5x, 366.41, 365.44, 362.83, 707.1x, 585.3, 585.4, 585.5, 585.6, 582.xx, 583.xx, 585.1, 585.2, 585.9, 586.xx, 587.xx, 642.1x, 250.4x, 250.40, 250.41, 250.42, 250.43, 403.xx, 404.xx, 572.4x, 580.xx, 584.xx, 580.0x, 580.4x, 580.89, 580.9x, 582.4x, 642.1x, 791.2x, 791.3x

Condition	US (MarketScan Research Database)	Nordic Registers	Israel (Maccabi Health Services Database)
	H34.8390, H34.8391, H34.8392, H35.31, H35.311, H35.3110, H35.3111, H35.3112, H35.3113, H35.3114, H35.312, H35.3120, H35.3121, H35.3122, H35.3123, H35.3124, H35.313, H35.3130, H35.3131, H35.3132, H35.3133, H35.3134, H35.319, H35.3190, H35.3191, H35.3192, H35.3193, H35.3194, H35.32, H35.321, H35.3210, H35.3211, H35.3212, H35.3213, H35.322, H35.3220, H35.3221, H35.3222, H35.3223, H35.323, H35.3230, H35.3231, H35.3232, H35.3233, H35.329, H35.3290, H35.3291, H35.3292, H35.3293, H36.0, H42., H43.1, H43.10, H43.11, H43.12, H43.13, I79.2, L97.201, L97.202, L97.203, L97.204, L97.205, L97.206, L97.208, L97.209, L97.211, L97.212, L97.213, L97.214, L97.215, L97.216, L97.218, L97.219, L97.221, L97.222, L97.223, L97.224, L97.225, L97.226, L97.228, L97.229, L97.301, L97.302, L97.303, L97.304, L97.305, L97.306, L97.308, L97.309, L97.311, L97.312, L97.313, L97.314, L97.315, L97.316, L97.318, L97.319, L97.321, L97.322, L97.323, L97.324, L97.325, L97.326, L97.328, L97.329, L97.401, L97.402, L97.403, L97.404, L97.405, L97.406, L97.408, L97.409, L97.411, L97.412, L97.413, L97.414, L97.415, L97.416, L97.418, L97.419, L97.421, L97.422, L97.423, L97.424, L97.425, L97.426, L97.428, L97.429, L97.501, L97.502, L97.503, L97.504, L97.505, L97.506, L97.508, L97.509, L97.511, L97.512, L97.513, L97.514, L97.515, L97.516, L97.518, L97.519, L97.521, L97.522, L97.523, L97.524, L97.525, L97.526, L97.528, L97.529, L97.801, L97.802, L97.803, L97.804, L97.805, L97.806, L97.808, L97.809, L97.811, L97.812, L97.813, L97.814, L97.815, L97.816, L97.818, L97.819, L97.821, L97.822, L97.823, L97.824, L97.825, L97.826, L97.828, L97.829, L97.901, L97.902, L97.903, L97.904, L97.905, L97.906, L97.908, L97.909, L97.911, L97.912, L97.913, L97.914, L97.915, L97.916, L97.918, L97.919, L97.921, L97.922, L97.923, L97.924, L97.925, L97.926, L97.928, L97.929, M14.2, M14.671, M14.672, M14.679, N08.3, Z86.31		
Cardiovascular Disease	**ICD-9:** 428.0, 428.1, 428.20, 428.21, 428.22, 428.23, 428.30, 428.31, 428.32, 428.33, 428.40, 428.41, 428.42, 428.43, 428.9, 410.00, 410.01, 410.02, 410.10, 410.11, 410.12, 410.20, 410.21, 410.22, 410.30, 410.31, 410.32, 410.40, 410.41, 410.42, 410.50, 410.51, 410.52, 410.60, 410.61, 410.62, 410.70, 410.71, 410.72, 410.80, 410.81, 410.82, 410.90, 410.91, 410.92, 411.0, 411.1, 411.81, 411.89, 412, 413.0, 413.1, 413.9, 414.00, 414.01, 414.02, 414.03, 414.04, 414.05, 414.06, 414.07, 414.10, 414.11, 414.12, 414.19, 414.2, 414.3, 414.4, 414.8, 414.9, 427.31, 427.32 **ICD-10:** I20.0, I20.1, I20.8, I20.9, I21.01, I21.02, I21.09, I21.11, I21.19, I21.21, I21.29, I21.3, I21.4, I21.9, I21.A1, I21.A9, I22.0, I2.21, I2.22, I2.28, I2.29, I24.0, I24.1, I2.48, I2.49, I25.10, I25.110, I25.111, I25.118, I25.119, I25.2, I25.3, I2.541, I25.42, I2.55, I25.6, I25.700, I25.701, I25708, I25.709, I25.710, I25.711, I25.718, I25.719, I25.720, I25.721, I25.728, I25.729, I25.730, I25731, I25.738, I257.39, I25.750, I25.751, I25.758, I25.759, I25.760, I25.761, I25.768, I25.769, I25790, I25.791, I25.798, I25.799, I25.810, I25.811, I25.812, I25.82, I25.83, I25.84, I25.89, I25.9, I480, I481, I48.2, I48.3, I48.4, I48.91, I48.92, I50.1, I50.20, I50.21, I50.22, I50.23, I50.30, I50.31, I50.32, I50.33, I50.40, I5.041, I50.42, I50.43, I50.810, I50.811, I50.812, I50.813, I50.814, I50.82, I50.83, I50.84, I508.9, I50.9	**ICD-10:** I20-I25, I48, I50, I61-I66, I69.1-I69.4, I70-I72, I73.9, I74	At least two diagnoses (ICD-9) for one of the following cardiovascular disease groups: ischemic heart disease (410.x–414.x), congestive heart failure (428.x), vascular disease and atherosclerosis (440.x-447.x, 557.x), arrhythmias and conduction disorders (426.x-427.x), pericardium and endocardium diseases (423.x-424.x); Chronic rheumatic heart disease(391.x, 393.x-398.x), cardiomyopathic diseases (425.x), hypertensive heart disease (402.x,404.x), inflammatory heat conditions (393.x, 398.x,420.x-422.x) pulmonary heart disease (415.x-416.x); other heart conditions (429.x, 794.x, 785.x); Cerebrovascular disease (430.x–438.x); congenital heart anomalies (745.x-747.x); Benign and malignant heart neoplasm (212.7, 164.1)
Polycystic ovary syndrome	**ICD-9:** 256.4x **ICD-10:** E28.2x	**ICD-10:** E28.2	**ICD-9:** 256.4x
Prescription medications	≥1 dispensation in maternal record from LMP-90 to LMP+90	≥1 dispensation in the prescribed drug registers from LMP-90 to LMP+97	Assessment period = LMP-180 to LMP+90
Antihypertensives	NDC codes	ATC codes:C02 (antihypertensives), C03 (diuretics), C07 (beta blockers), C08 (calcium channel blockers)	ATC codes:C02 (antihypertensives), C03 (diuretics), C07 (beta blockers), C08 (calcium channel blockers)
Lipid modifying agents	NDC codes	ATC codes: C10	ATC codes: C10

Abbreviations: ATC code, Anatomical Therapeutic Chemical code; BMI, body mass index; Cat, category; ICD, International Classification of Diseases; LMP, last menstrual period; n/a, not available; NDC, national drug code.

Supplementary Table 6. Mean and Median HbA_{1c} for the full study population and women with pre-gestational type 2 diabetes mellitus with different periconceptional antidiabetic medication use in a subset of the US MarketScan and Israel Maccabi Health Services databases

	US - MarketScan				Israel -MHS			
	n [1]	% of total population with HbA1c values	mean (SD)	median (IQR)	n [1]	% of total population with HbA1c values	mean (SD)	median (IQR)
All pregnancies	6286	0.9%	5.4 (0.7)	5.3 (0.4)	31686	8.5%	5.2 (0.4)	5.2 (0.4)
T2DM	397	4.3%	6.7 (1.6)	6.1 (1.5)	575	58.2%	6.0 (0.9)	5.8 (0.8)
No ADM	127	2.6%	5.9 (1.1)	5.7 (0.8)	165	53.1%	5.8 (0.7)	5.7 (0.7)
Metformin only	87	6.1%	6.3 (1.1)	6.0 (1.1)	90	61.6%	5.9 (0.8)	5.8 (0.7)
Insulin	64	5.1%	7.8 (2.0)	7.2 (2.9)	253	60.0%	6.0 (0.8)	5.8 (0.8)
Sulfonylureas	81	8.1%	7.1 (1.7)	6.5 (1.8)	60	52.2%	6.0 (1.1)	5.7 (0.6)
DDP-4 inhibitors	23	7.2%	7.8 (1.8)	7.6 (2.6)	55	68.8%	6.7 (1.1)	6.5 (1.6)
GLP1 receptor agnists	35	6.2%	7.0 (1.7)	6.7 (2.6)	19	44.2%	6.0 (0.9)	5.8 (0.9)
SGLT2 inhibitors	13	7.6%	8.0 (2.5)	7.4 (3.2)	25	71.4%	6.7 (1.2)	6.6 (1.5)

Abbreviations: ADM, antidiabetic medication; T2DM, type 2 diabetes mellitus; DPP4, Dipeptidyl peptidase 4; GLP-1, Glucagon-like peptide-1; SGLT2, Sodium-glucose co-transporter 2; SD, standard deviation; IQR, interquartile range.

[1] number of women with a recorded HbA1c value

For the US:

Only a subsample (around 7%) of MarketScan enrollees has laboratory data available in the Research Database, i.e., a higher proportion of pregnancies had HbA1c tests, but they are not available to investigators.

Pregnancies with at least one LOINC code for HbA_{1c} test within LMP-90 to LMP+90 were identified.

Logical Observation Identifier Names and Codes (LOINC) for HbA_{1c} test results: 4548-4, 17856-6, 17855-8, 4549-2, 55454-3.

Any lab values outside the range allowed (2-20 units), re-coded as missing.

For Israel:

Pregnancies with at least one HbA_{1c} test within LMP-90 to LMP+90 were identified.

For both US and Israel:

- If more than 1 HbA_{1c} value during the assessment period, the one closest to the LMP was selected
- If more than 1 HbA_{1c} test was taken on the same date, the average of values was calculated
- If any 2 HbA_{1c} tests are of equal distance in time (days) from LMP, the average of the values was calculated

Supplementary Table 7. Prevalence and 95% confidence intervals of any and cardiac major congenital malformation in live-born infants in the full pregnancy cohort and born to women with type 2 diabetes mellitus with periconceptional use of no antidiabetic medication, metformin only, insulin, or 2nd-line non-insulin antidiabetic medications

		Any Major Congenital Malformation		Cardiac Malformations	
	Number of exposed	Number of cases	Pooled prevalence, % (95% CI)	Number of cases	Pooled prevalence, % (95% CI)
All Pregnancies	3514865	132283	3.76 (3.74-3.78)	45988	1.31 (1.30-1.32)
All T2DM	51826	2584	5.28 (5.04-5.53)	1115	2.25 (2.09-2.41)
No ADM	36678	1602	4.77 (4.42-5.12)	858	2.30 (2.07-2.53)
Metformin only	7440	377	5.32 (4.68-5.95)	141	2.04 (1.62-2.46)
Insulin	5078	400	7.83 (7.09-8.57)	212	4.20 (3.64-4.76)
Sulfonylureas	1362	121	9.71 (6.80-12.62)	50	4.85 (2.65-7.04)
DPP4 inhibitors	687	50	6.14 (4.15-8.14)	24	3.26 (1.75-4.78)
GLP-1 receptor	938	75	8.23 (5.58-10.88)	23	3.22 (1.43-5.01)
agnists SGLT2 inhibitors	335	30	7.04 (3.35-10.73)	15	3.88 (1.01-6.75)

Abbreviations: ADM, antidiabetic medication; T2DM, type 2 diabetes mellitus; DPP4, Dipeptidyl peptidase 4; GLP-1, Glucagon-like peptide-1; SGLT2, Sodium-glucose co-transporter 2.

Supplementary Table 8. Crude and adjusted relative risks and 95% confidence intervals for any and cardiac major congenital malformations in infants born to women with type 2 diabetes mellitus and periconceptional use of 2nd-line non-insulin antidiabetic medication compared with insulin, presented separately for the Nordic countries (pooled Finland, Iceland, Norway, Sweden), US MarketScan, and Israel Maccabi Health Services databases

	Any Major Congenital Malformation			Cardiac Malformation		
	No. exposed cases / No. exposed (%)	Crude Relative Risk (95%CI)	Adjusted Relative Risk (95% CI) [a]	No. exposed cases / No. exposed (%)	Crude Relative Risk (95%CI)	Adjusted Relative Risk (95% CI) [a]
Nordic						
Insulin	256/3269 (7.8)	reference	reference	151/3269 (4.6)	reference	reference
Sulfonylureas	20/198 (10.1)	1.29 (0.84-1.99)	1.32 (0.85-2.05)	11/198 (5.6)	1.20 (0.66-2.18)	1.19 (0.65-2.16)
DPP4 inhibitors	14/266 (5.3)	0.67 (0.40-1.13)	0.67 (0.39-1.14)	8/266 (3.0)	0.65 (0.32-1.31)	0.64 (0.32-1.30)
GLP-1 receptor agnists	16/214 (7.5)	0.95 (0.57-1.59)	1.02 (0.60-1.73)	8/214 (3.8)	0.81 (0.38-1.74)	0.91 (0.41-2.04)
SGLT2 inhibitors	5/82 (6.1)	0.78 (0.33-1.82)	0.85 (0.35-2.02)	<5/82	0.79 (0.26-2.40)	0.93 (0.31-2.79)
US-MarketScan						
Insulin	115/1387 (8.3)	reference	reference	48/1387 (3.5)	reference	reference
Sulfonylureas	90/1049 (8.6)	1.04 (0.78-1.38)	1.10 (0.82-1.47)	35/1049 (3.3)	0.96 (0.62-1.49)	0.97 (0.62-1.51)
DPP4 inhibitors	32/341 (9.4)	1.15 (0.76-1.72)	1.18 (0.79-1.78)	13/341 (3.8)	1.11 (0.59-2.06)	1.12 (0.60-2.08)
GLP-1 receptor agnists	53/681 (7.8)	0.93 (0.67-1.31)	0.85 (0.59-1.22)	14/681 (2.1)	0.59 (0.32-1.07)	0.57 (0.29-1.09)
SGLT2 inhibitors	23/218 (10.6)	1.30 (0.81-2.09)	1.05 (0.65-1.70) [b]	11/218 (5.0)	1.48 (0.76-2.90)	1.21 (0.61-2.40) [b]
Israel - MHS						
Insulin	29/422 (6.9)	reference	reference	13/422 (3.1)	reference	reference
Sulfonylureas	11/115 (9.6)	1.39 (0.72-2.70)	1.33 (0.68-2.60)	4/115 (3.5)	1.13 (0.37-3.40)	1.14 (0.39-3.34)
DPP4 inhibitors	4/80 (5.0)	0.73 (0.26-2.02)	0.66 (0.24-1.84)	3/80 (3.8)	1.22 (0.35-4.18)	1.10 (0.32-3.78)
GLP-1 receptor agnists	6/43 (14.0)	2.03 (0.89-4.41)	1.69 (0.64-4.44)	1/43 (2.3)	0.75(0.10-5.63)	0.64 (0.09-4.59)
SGLT2 inhibitors	2/35 (5.7)	0.83 (0.21-3.35)	0.73 (0.18-2.98)	1/35 (2.9)	0.93 (0.12-6.90)	0.83 (0.11-6.50)

Counts <5 are not shown for data privacy policies in the Nordics

[a] Adjusted for birth year, maternal age, obesity, and specific Nordic country (in the pooled Nordic cohort only)

[b] Adjusted for birth year and obesity

Abbreviations: CI, confidence intervals; DPP4, Dipeptidyl peptidase 4; GLP-1, Glucagon-like peptide-1; SGLT2, Sodium-glucose co-transporter 2.

Supplementary Table 9. Crude relative risks and 95% confidence intervals for any and cardiac major congenital malformation in infants born to women with type 2 diabetes mellitus and first trimester use of 2nd-line non-insulin antidiabetic medications compared with insulin, presented meta-analyzed and separately for the Nordic countries (pooled Finland, Iceland, Norway, Sweden), US MarketScan, and Israel Maccabi Health Services databases

	Any Major Congenital Malformation		Cardiac Malformation	
	No. exposed cases / No. exposed (%)	Crude Relative Risk (95%CI)	No. exposed cases / No. exposed (%)	Crude Relative Risk (95%CI)
All				
Insulin	412/5194 (7.8 [a])	reference	218/5194 (4.2 [a])	reference
Sulfonylureas	88/1070 (9.1 [a])	1.02 (0.79-1.32)	35/1070 (3.2 [a])	0.89 (0.6-1.33)
DPP-4 inhibitors	27/400 (5.8 [a])	0.82 (0.55-1.23)	10/400 (1.9 [a])	0.68 (0.35-1.31)
GLP-1 receptor agnists	38/461 (6.7 [a])	1.03 (0.73-1.47)	8/461 (1.6 [a])	0.46 (0.22-0.94) [b]
SGLT2 inhibitors	15/181 (4.3 [a])	1.20 (0.69-2.11) [b]	7/181 (1.2 [a])	1.56 (0.70-3.50) [c]
Nordic				
Insulin	245/3164 (7.7)	reference	147/3164 (4.7)	reference
Sulfonylureas	9/98 (7.7)	1.19 (0.63-2.24)	<5/98	0.66 (0.21-2.03)
DPP-4 inhibitors	7/134 (5.2)	0.67 (0.32-1.40)	<5/134	0.32 (0.08-1.28)
GLP1 receptor agnists	5/110 (4.6)	0.59 (0.25-1.40)	<5/110	0.39 (0.1-1.56)
SGLT2 inhibitors	<5/36	0.36 (0.05-2.49)	0/36	no exposed cases
US-MarketScan				
Insulin	136/1583 (8.6)	reference	58/1583 (3.7)	reference
Sulfonylureas	68/870 (7.8)	0.90 (0.67-1.22)	28/870 (3.2)	0.87 (0.55-1.39)
DPP4 inhibitors	18/224 (8.0)	0.93 (0.56-1.55)	7/224 (3.1)	0.85 (0.38-1.88)
GLP-1 receptor agnists	30/331 (9.1)	1.06 (0.70-1.61)	6/331 (1.8)	0.49 (0.21-1.14)
SGLT2 inhibitors	14/125 (11.2)	1.34 (0.75-2.41)	7/125 (5.6)	1.56 (0.70-3.50)
Israel-MHS				
Insulin	31/447 (6.9)	reference	13/447 (2.9)	reference
Sulfonylureas	11/102 (6.9)	1.56 (0.81-2.99)	4/102 (3.9)	1.35 (0.45-4.05)
DPP4 inhibitors	2/42 (4.8)	0.69 (0.17-2.77)	1/42 (2.4)	0.82 (0.11-6.11)
GLP-1 receptor agnists	3/20 (15.0)	2.16 (0.72-6.45)	0/20	no exposed cases
SGLT2 inhibitors	0/20	no exposed cases	0/20	no exposed cases

Counts <5 are not shown for data privacy policies in the Nordics

[a] Standardized prevalence

[b] No exposed cases in Israel, includes only Nordic and US estimates

[c] No exposed cases in Israel or the Nordics

Abbreviations: CI, confidence intervals; DPP4, Dipeptidyl peptidase 4; GLP-1, Glucagon-like peptide-1; SGLT2, Sodium-glucose co-transporter 2.

Supplementary Methods 1. Description of Nordic Data and Ethical Approval Information.

Description of the Nordic databases

Similar health and social registers exist in Finland, Iceland, Norway, and Sweden, which are linkable by a personal identity number assigned to all residents of each country. The Nordic countries all have publicly funded healthcare systems with reporting to the registers mandated by law.

For more information on the Nordic Health registers, see the publication by Laugesen and colleagues.(4)

Finland

- The **Finnish Medical Birth Register** was established in 1987. The registry includes data on all live births and stillbirths of at least 500 grams or 22 completed gestational weeks, as well as data on mothers.
- **Register of Reimbursed Drug Purchases and Register of Medical Special Reimbursements**. Nationwide databases on reimbursed drug purchases available from 1995. If an individual is entitled to special reimbursement, then drug refill is accompanied with indication for which the prescription was reimbursed.
- The **Finnish Patient Register - Care Register for Health care (HILMO)** contains dates of hospitalizations and visits, all diagnoses (ICD codes) and surgical procedures (NCSP codes) from inpatient care in all hospitals since 1967 and outpatient specialist care in public hospitals since 1998.
- **Finnish Register of Congenital Anomalies** contains all malformations (including terminations and stillbirths) identified within one year of birth, which have been validated based on hospital records. (https://thl.fi/en/web/thlfi-en/statistics/information-on-statistics/quality-descriptions/congenital-anomalies)

Iceland

- **Icelandic Medical Birth Register**: Since 1981, mandatory registration of all live- and stillbirths of at least 500 grams or 22 completed gestational weeks.
- **Icelandic Prescription Medicines Register**: Since 2003, mandatory registration of all outpatient drugs dispensed in Iceland. Prescription drugs administered to individuals in nursing homes are included after from 2011 onwards.
- The **Icelandic Patient Register:** Contains dates of hospitalizations and visits, all diagnoses (ICD codes) and surgical procedures (NCSP codes) from hospital inpatient stays since 1999 and outpatient wards since 2010.
- **Statistics Iceland**: Highest obtained level of education categorized on an annual basis according to the International Standard Classification of Education (ISCED).

Norway

- **Medical Birth Registry of Norway (MBRN):** Since 1967, mandatory registration of all live- and stillbirths from 16 completed gestational weeks. Includes all pregnancy terminations after 12 weeks for fetal anomaly (TOPFA) since 1999. Includes data from Neonatal Intensive Care Units, including neonatal and major congenital malformation diagnoses, for all infants transferred to such units after birth since 1999.
- **Norwegian Prescription Database (NorPD):** Since January 2004, mandatory registration of all drugs dispensed in Norway. Dispensed drugs are recorded according to the Anatomical Therapeutic Chemical (ATC) classification system, with the date of dispensation, the strength, and quantity Since 2008, includes ICD-10 or ICPC-2 diagnosis for drugs dispensed for chronic conditions. Before 2008, another reimbursement coding system was used. Drugs administered in hospitals or nursing homes are not included.
- **Norwegian Patient Registry (NPR):** Since 2008, dates, ICD-10 diagnoses, and procedures (NCSP codes) from all public specialists' health-care services (both inpatient and outpatient care), including private institutions contracted to the regional health authorities.
- **Norwegian Population Register (National Registry):** Migration/moving, marriage and cohabitation

Sweden

- **The Swedish Medical Birth Register** covers since 1973, 99% of all live- and stillbirths from gestational week 22. Before July 1,2008 stillbirths occurring from week 28 only were included. Data is collected from antenatal care clinics, delivery units and pediatric examination of the infant.
- **The Swedish Prescribed Drug Register** was established in July 2005 and contains complete national data on all pharmaceuticals dispensed on prescription. Drugs are recorded according to the Anatomical Therapeutic Chemical (ATC)

classification system, with the date of dispensation, the strength, and quantity. Drugs administered in hospitals or nursing homes are not included.

- **The Swedish Patient Register** contains dates of hospitalizations and visits, all diagnoses (ICD codes) and surgical procedures (NCSP codes) from inpatient stays. The reporting started in 1964 and since 1987, the register has covered all public, inpatient care in Sweden. Since 2001 both public and private care is included in the register and since 2002 there is almost full coverage of all outpatient hospital visits.

Ethical boards providing approval for data use & approval numbers

Country	Ethical Board	Approval Number
Finland	No Ethical Board approval needed.	THL/1551/6.02.00/2018, THL/1673/5.05.00/2019, Kela 117/522/2019
Iceland	National Bioethics Committee	VSNb2018060017/03.01
Norway	Regional Committee for Medical Research Ethics South/East Norway The Norwegian Data Inspectorate in Norway	2017/2546/REC South-East 17/02068/Norwegian Data Inspectorate
Sweden	Swedish Ethical Review Authority (Etikprövningsmyndigheten)	dnr 2015/1826-31/2, 2017/2238-32, 2018/1790-32, 2018/2211-32, 2022-04004-02

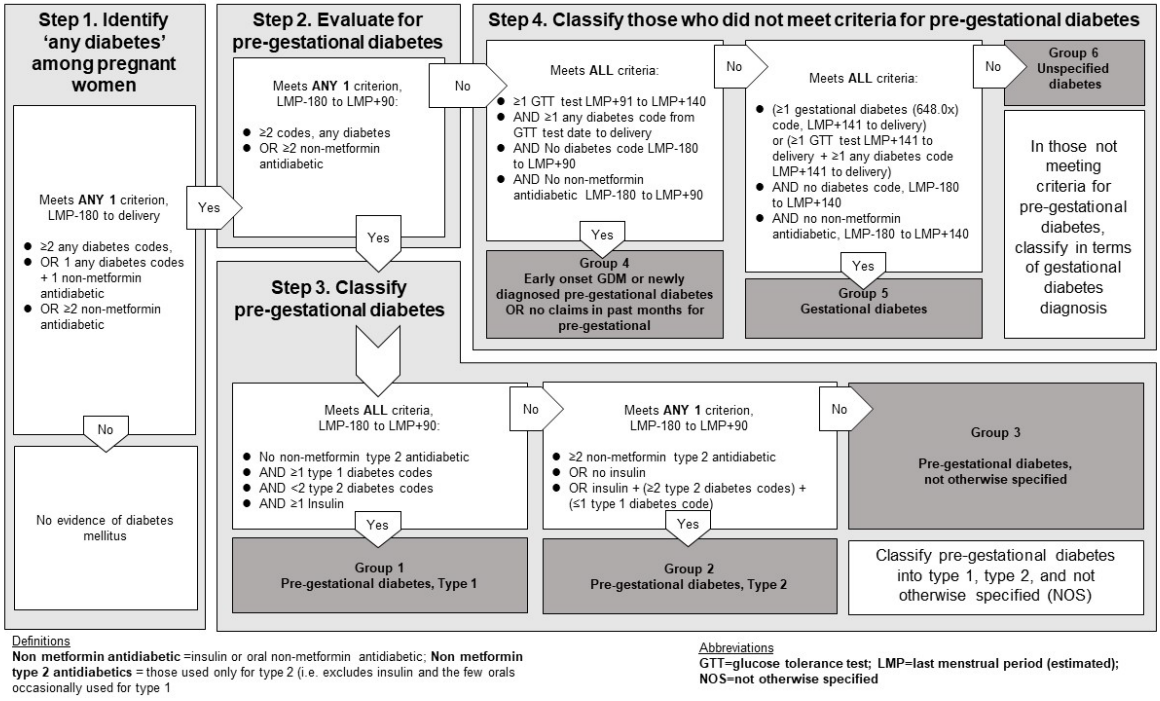
Supplementary Methods 2: Pre-gestational Diabetes Algorithms

a. **US cohort –** Pregnant women with a pre-gestational T2DM were identified using a validated algorithm developed by Wood et al.,(2021)(5)

Summary of algorithm:

1) *Identify any diabetes*
2) *Evaluate for pre-gestational diabetes*
3) *Rule out Type 1 diabetes*
4) *Type 2 diabetes: Meets ANY 1 criterion LMP-180 to LMP+90:*
   - *≥2 filled prescriptions of non-metformin type 2 antidiabetic drug (i.e., excludes insulin and the few oral drugs occasionally used for type 1 DM)*
   - *0 filled prescriptions for insulin*
   - *(≥ 1 filled prescription for insulin) + (≥2 type 2 diabetes codes) + (≤1 type 1 diabetes codes)*

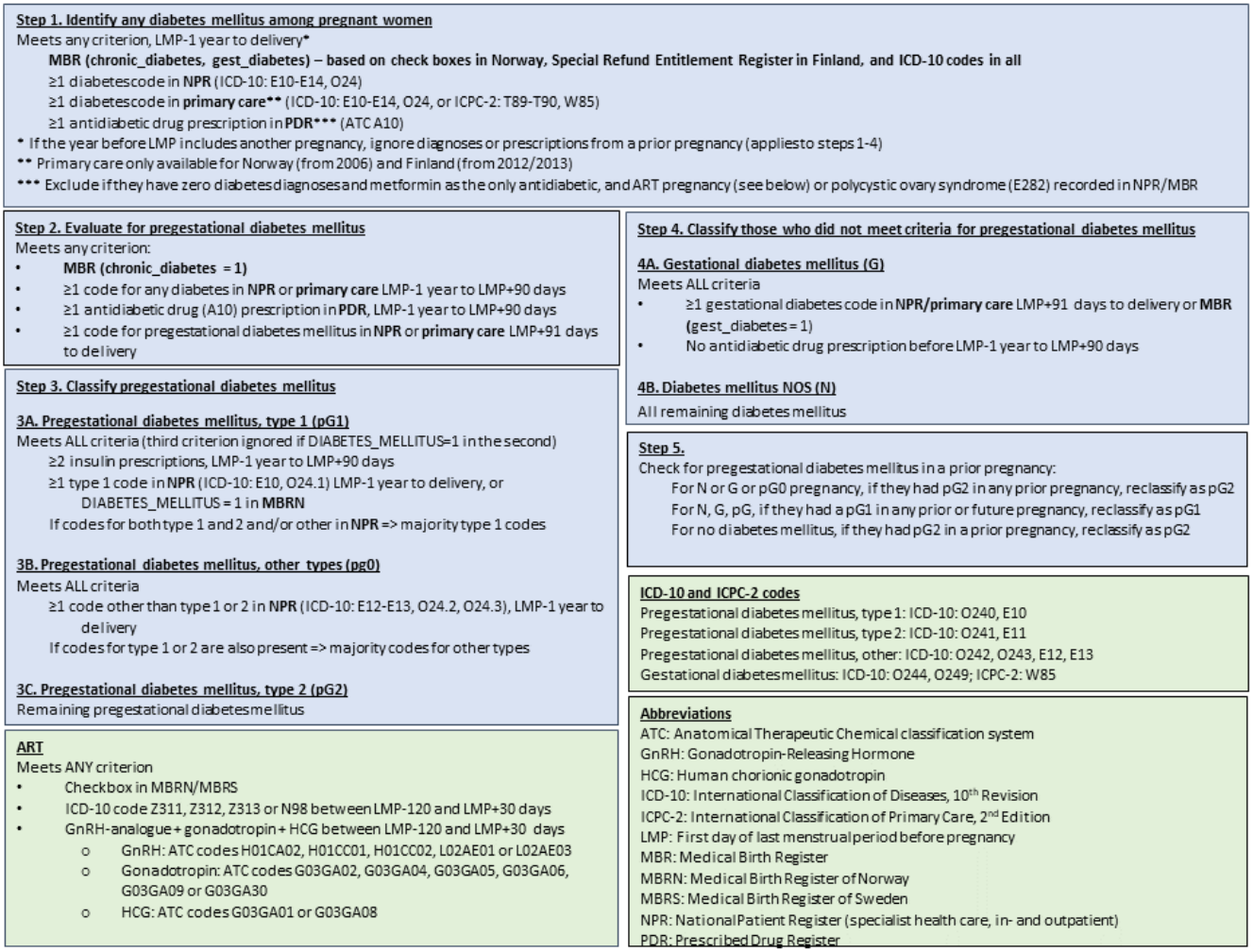
ICD-9-CM	ICD-10	Definition
250.x1, 250.x3	O24.0x, O24.0xx, E10.x, E10.xx, E10.xxx, E10.xxxx	**Type 1 pre-gestational diabetes**
250.x0, 250.x2	O24.1x, O24.1xx, E11.x, E11.xx, E11.xxx, E11.xxxx	**Type 2 pre-gestational diabetes**



b. **Nordic** – Algorithm used for pooled data from Finland, Iceland, Norway, and Sweden

Summary of algorithm:

1) *Identify any diabetes (LMP-1 year to delivery)*
2) *Evaluate for pre-gestational diabetes (LMP-1 year to LMP+90) including medication*
3) *Rule out Type 1 diabetes and other types of pre-gestational diabetes*
4) *Type 2 diabetes are the remaining pre-gestational diabetes cases*



c. **Israel** – pregnant women with pre-gestational T2DM were identified by inclusion into the Maccabi Health Services diabetes register,(6) according to the following criteria:

Criteria for the diabetes registry

1. HbA1c ≥ 7.25%
2. At least two random glucose tests ≥200 mg/dl with a minimum gap of 30 days between tests.
3. Oral drugs: Purchase of at least two oral medications for diabetes in a three-month period, with one of the following: A) at least one glucose test above 125 mg/dl; B) HbA1c ≥ 6.5%.
   . Purchase of oral medications on the same day counts as only one purchase
   . A woman of childbearing age (18-55 years) with a GCT or GTT test (no matter the value), whose last purchase of an oral antidiabetic drug was within less than four months from the data of the test does not enter the registry (added to the gestational diabetes registry).
4. Insulin: Purchase of at least two insulin medications in a three-month period.
   a. A patient who entered the registry based on dispensing of insulin alone and who did not have additional dispensing records for insulin in the 6 consecutive months following the initial dispensing date is removed from the registry.
   b. Purchase of multiple insulin drugs on the same day counts as only one purchase
   c. A woman of childbearing age (18-55 years) with a GCT or GTT test (no matter the value), whose last purchase date of insulin was within less than four months from the date of the test does not enter the registry (added to the gestational diabetes registry).
5. Diabetes related diagnoses: diagnosis recorded by a family physician/ pediatrician, diabetes consultant, endocrinologist, or ophthalmologist, with one of the following:
   a. A. HbA1c≥ 6.5% within six months before or after diagnosis
   b. Two glucose tests > 125 mg/dl, one six months before or after diagnosis and one at any point in time.

Determining type of diabetes:

- Type 1 diabetes –
  . Added to the registry at age ≤ 26
  . Purchased insulin 5 or more times, and did not purchase other oral medications, or if other oral medications were purchased, first purchase occurred after at least 5 consecutive insulin purchases and after at least 1 year in the registry.
- Type 2 diabetes –
  . Patients in the registry who did not purchase insulin for at least 3 years from the time they entered the registry.
  . Patients who discontinued insulin and started therapy with other oral medications for diabetes who were treated with oral medications for at least 3 years after discontinuation of insulin (last oral purchase date - last insulin purchase date> 3 years).
  . Patients who received both insulin and oral medications for diabetes, conditional that the oral medications were initially received at least 3 years before insulin onset (first insulin purchase date - first oral purchase date> 3 years).

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