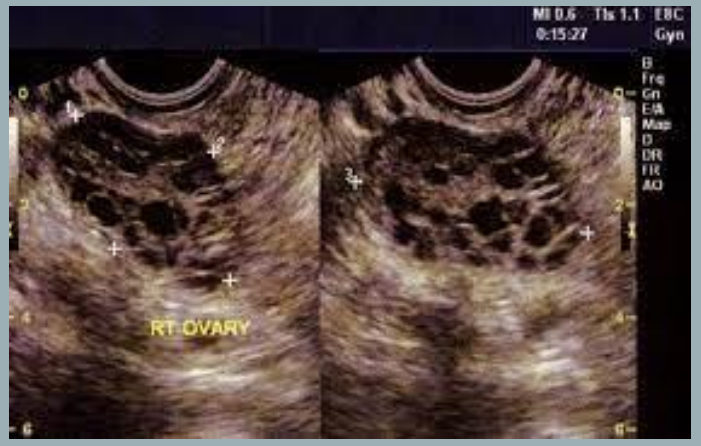


PCOS, DIABETES AND BREASTFEEDING

Dr Kate Rassie, MBChB FRACP

Endocrinologist, Monash Health and Jean Hailes for Women's Health

PhD Candidate, Monash Centre for Health Research and Implementation, Monash University

Neuroprotective Developmental Care Lactation Fellowship 2024: Endocrinology Session 1

I have no actual or potential conflicts of interest to declare in relation to this talk.

AN AGENDA

- What are the proposed maternal metabolic benefits of breastfeeding for women with GDM?
- What caution do we need to have in interpreting this research?

- What difficulties might women with GDM or T2DM face in the post-partum?
- What interventions might help prepare women with GDM or T2DM for lactation?

- Is diabetic milk "full of sugar"?
- Does insulin enter breastmilk?

- What are the thoughts about the links between PCOS and breastfeeding?
- What are the key considerations for breastfeeding women with Type 1 diabetes?

CASE ONE

Anusha, 34F

G1P0

34/40, GDM diagnosed at 26 weeks

4.8 / 11.0* / 9.2* on 75g OGTT (<5.1 / <10.0 / <8.5)

Modified diet – switched to multigrain bread, reduced rice and pasta portions, walking 15 min after each meal

Currently requiring 4u Novorapid with lunch and dinner meals

Been (correctly, but confrontingly!) told her lifetime risk for T2DM may be as high as **50-60%**

Do women with GDM manage to breastfeed successfully?

YES!

Subtle differences only in BF outcomes between women with and without GDM - vary according to study setting

- Recent SR of 16 studies [1]:

- Overall probably NO differences in **BF initiation**

- SOME studies suggest reduced rates of exclusive BF at hospital discharge, and reduced durations of exclusive BF, in GDM women; but these are inconsistent and effect size small

[1] Nguyen PTH et al, Asia Pac J Public Health, 2019;31(3):183-198.

Will breastfeeding help reduce my risk of developing type 2 diabetes?

YES!

Lactation **consistently** associated with significantly reduced maternal risk of developing T2DM.
Probably ~30% ↓ [1]

Similar findings apply to women after GDM pregnancy.

[1] Rameez et al, JAMA Network Open. 2019;2(10):e1913401

Feng et al, J Diabetes Investig. 2018; 9:1360-1369.

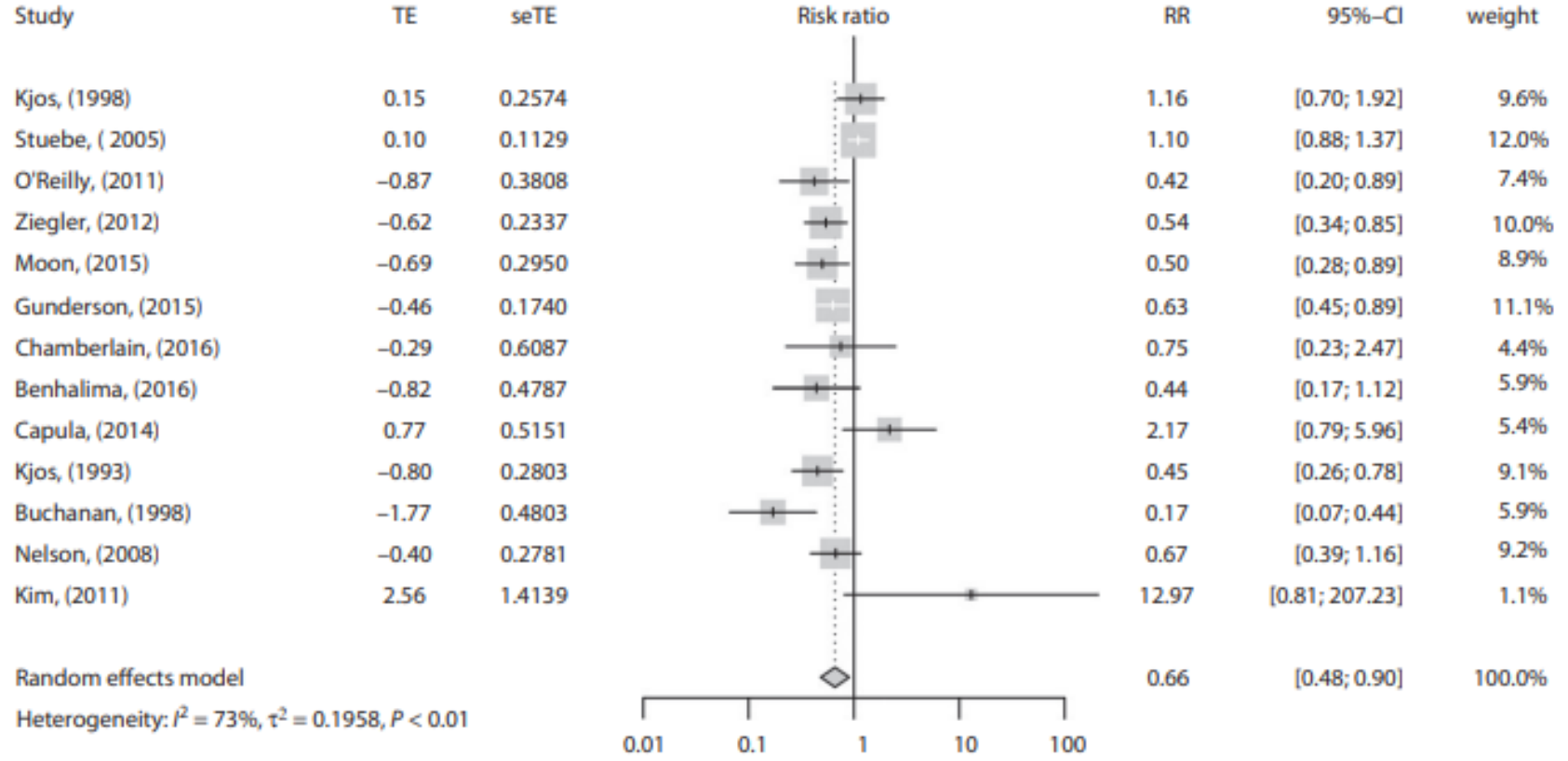


Figure 2 | Forest plot of studies showing the relative risk (RR) for the association between lactation and type 2 diabetes mellitus risk. CI, confidence interval; seTE, standard error of the log risk ratio; TE, transformation of relative risk.

One recent SR and MA of 13 cohort studies found that RR for T2DM development was **0.66** among women who **BF after a GDM pregnancy** (when compared with those who did not), 95% CI 0.48-0.90.

Sounds great!

What's the mechanism for that?

WHAT EXPLAINS THESE FINDINGS?

HOW DOES LACTATION IMPROVE MATERNAL METABOLISM AFTER GDM?

The "reset hypothesis" =

During pregnancy, visceral fat accumulates; insulin resistance increases; and lipid and triglyceride levels increase.

These changes all reverse more quickly, and more completely, with lactation.

The "reset hypothesis"

1. Lactation may reduce **maternal adiposity**

- In rats,

- fat deposition increases during pregnancy

- with lactation, stored lipids mobilised from adipose → mammary tissue → milk

- lactating animals have **smaller adipose cells and lower LPL activity than non-lactating controls**

- changes persist after lactation – even 21 days post-weaning, **rats who lactated have significantly less fat cells than those who didn't**

Stuebe et al, Am J Perinatol 2009; 26(1):81-88.

The "reset hypothesis"

1. Lactation may reduce **maternal adiposity**

- In humans, direct impact of lactation on post-partum weight change difficult to test – too many factors at play, esp dietary intake and energy expenditure

- Extra 400-500kcal/ 24h of expenditure for first 6mo if EBF
- Several studies have suggested that, in well-nourished contexts;

- BF women in the first 3 months post-partum probably ↑ calories and ↓ activity to meet energy demands of lactation,

- whereas **beyond 3mo,** lactating women more likely to mobilise fat stores.

- MRI and skinfold studies show that prolonged lactation is associated with mobilisation of fat from the supra-iliac and mid-thigh regions (compared with non-lactating controls).

Stuebe et al, Am J Perinatol 2009; 26(1):81-88.
Gunderson, Curr Diab Rep 2014; 14(2): 460.

The "reset hypothesis" =

2. Lactation helps **re-establish glucose homeostasis after delivery**

Table 2. Glucose Values and Diabetes Mellitus in Lactating and Nonlactating Women With Recent Gestational Diabetes

		n=404 Lactating	n=405 Nonlactating	*P*
Area under the curve (g · min/dL)		17.0 ± 4.2	17.9 ± 5.0	.01*
Fasting glucose	(mmol/L)	5.2 ± 0.7	5.4 ± 0.9	.0001*
2-hour glucose	(mmol/L)	6.9 ± 2.3	7.4 ± 2.7	<.01*
Diabetes mellitus†		17 (4.2%)	38 (9.4%)	.01

Data are presented as mean ± SD or *N* (%).
* Significant difference after adjusting for maternal age, body mass index, and insulin use during pregnancy.
† Diagnosed by the 2-hour oral glucose tolerance test as defined by the National Diabetes Data Group.[9]

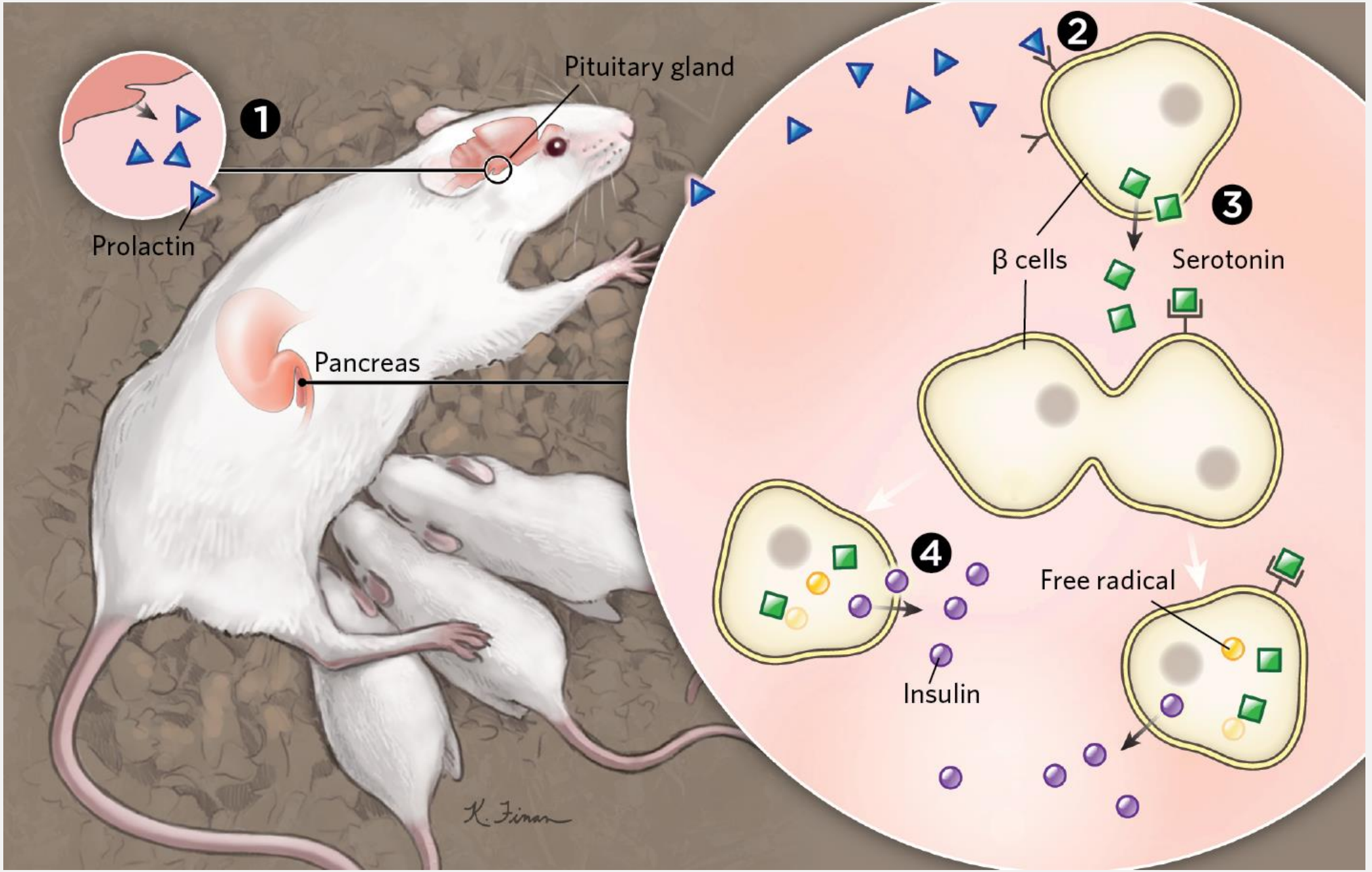
Kjos et al, Obstetrics and Gynaecology 1993: 82(3).

The "reset hypothesis" =

2. Lactation helps **re-establish glucose homeostasis after delivery**

- In women who BF, approximately **50g per day of glucose** is diverted to the mammary gland for milk production
- This glucose uptake is non-insulin-mediated!
- Lactating women thus have lower blood glucose and insulin concentrations despite higher rates of glucose production and lipolysis compared with non-lactating women
- Does this "unload" the pancreatic ß-cells, preserving long-term insulin production in these women?

Gunderson et al, Diabetes Care 2012: 35(50-56).



The Scientist, 2020

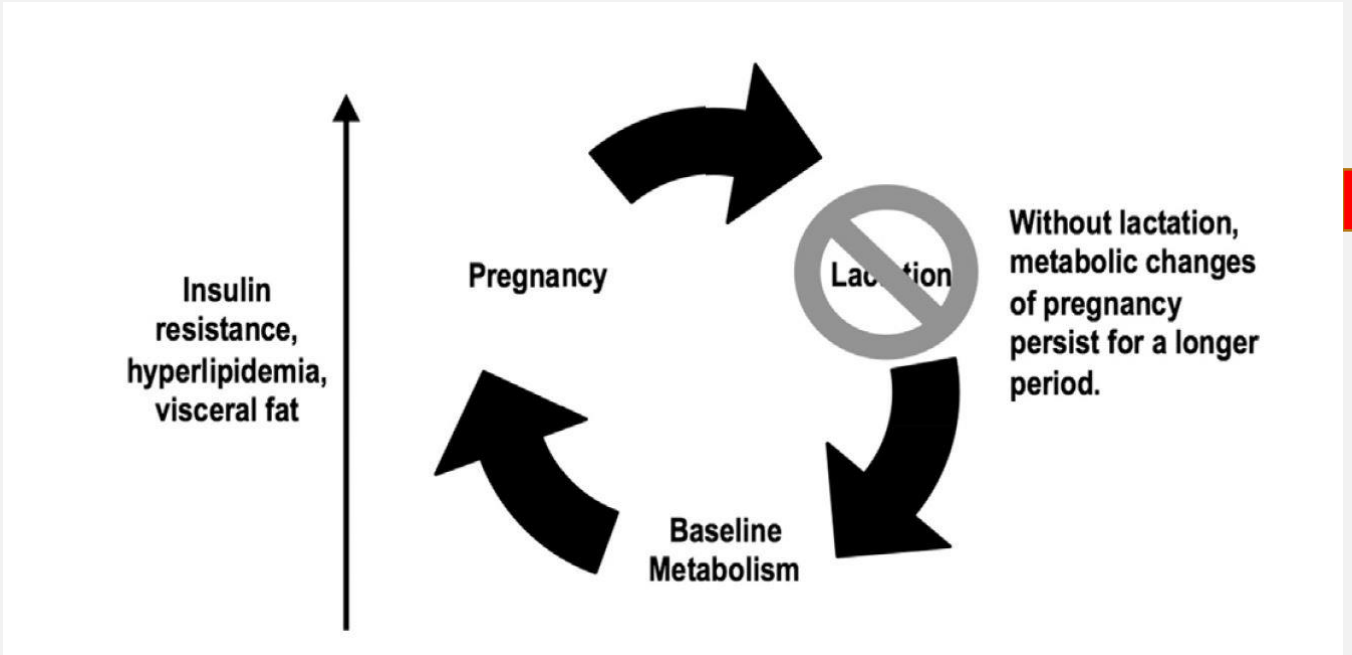
The "reset hypothesis" =

3. Lactation **has advantages for lipid homeostasis**

- Triglyceride and total cholesterol levels increase during human pregnancy, and fall after delivery
- This fall seems to be aided by lactation
- Multiple authors have documented lower LDL, lower Tg and higher HDL levels in lactating than non-lactating women; particularly with prolonged lactation

Stuebe et al, Am J Perinatol 2009; 26(1):81-88.

The "reset hypothesis" =



hence the findings of…

- ↓ GDM → T2DM
- ↓ metabolic syndrome
- ↓ hyperlipidemia
- ↓ HTN
- ↓ CV events

…in lactating women.

Stuebe, Seminars in Perinatology 2015, 39: 290-295.

BUT….

- ALL this (human) evidence is observational.
- "Lactating" groups are women **self-selected by their ability to breastfeed.**

- When we think critically about studies showing improved metabolic profiles in lactating women, we need to also consider

(a) Confounding – women who breastfeed are more likely to engage in other healthy behaviours

(b) Reverse causation – do the more favourable metabolic profiles consistently seen in lactating women simply reflect the fact that **metabolically healthy women are more able to breastfeed in the first place?**

WHAT EXPLAINS THESE FINDINGS?

HOW DOES LACTATION IMPROVE MATERNAL METABOLISM AFTER GDM?

The "preset hypothesis" =

Pre-existing maternal metabolic dysregulation impacts on lactation performance.

Observational evidence doesn't show that lactation improves maternal metabolism – rather, it shows that ***metabolically healthy women are more likely to successfully breastfeed.***

Adverse lactation outcomes may be a marker for underlying maternal cardiometabolic disease risk.

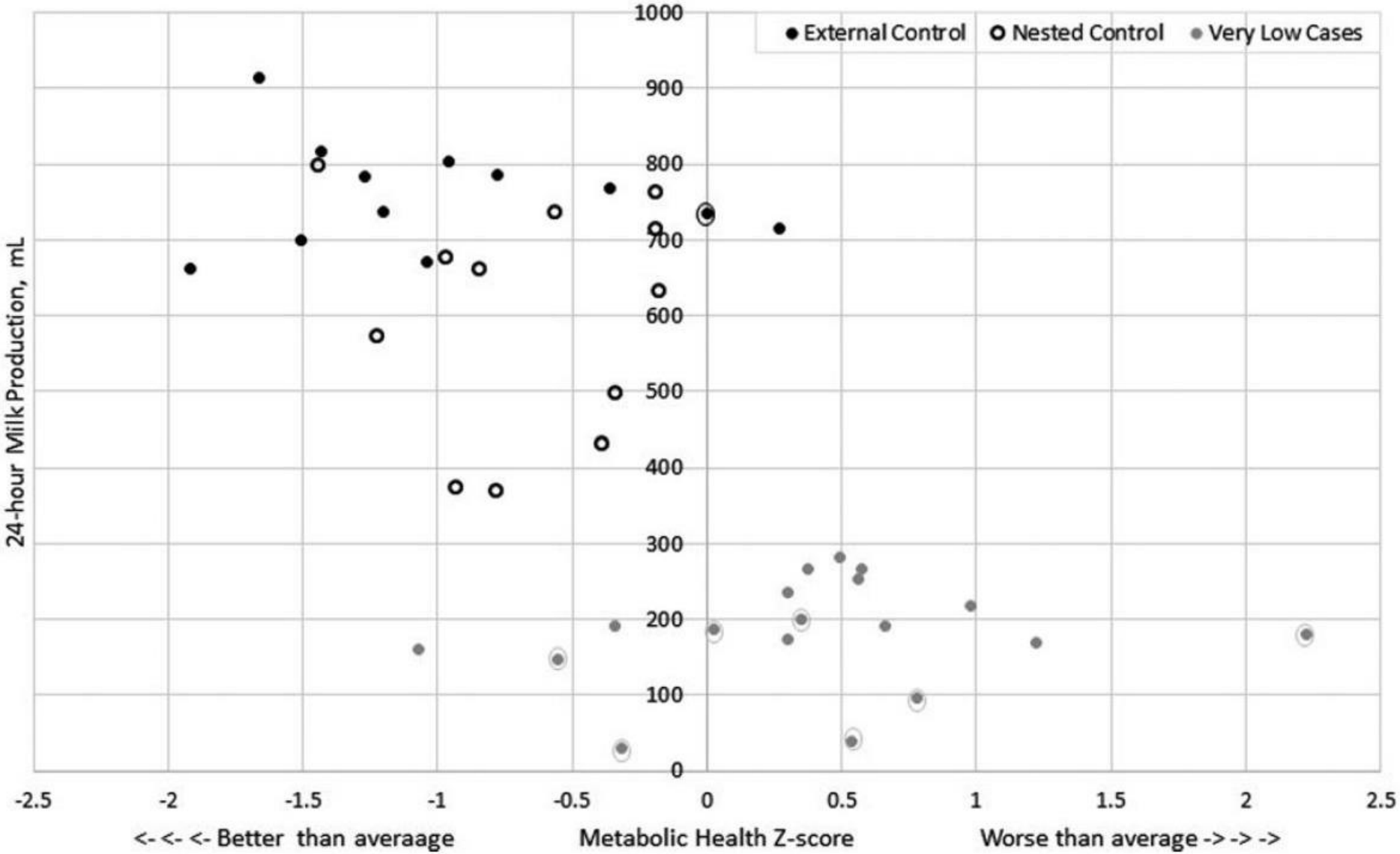


FIG. 2. Scatterplot of 24-hour milk production by Metabolic Syndrome Severity *z*-score, where 0, >0, and <0 *z*-scores signify average, worse than average, and better than average metabolic health profiles, respectively, as compared to all U.S. adults aged 20–65. *Solid black circles*: external control group, $n=12$; *Open black circles*: nested control group, $n=12$; *Solid gray circles*: severely low milk output cases, $n=18$. Encircled markers of any color indicate gestational diabetes mellitus diagnosis, $n=7$ cases and $n=1$ external control. GDM, gestational diabetes mellitus.

CASE TWO

Zara, 36F

BMI 39

Diagnosed with T2DM aged 32

When non-pregnant, metformin 1g BD and weekly Trulicity (dulaglutide) 1.5mg

Basal-bolus insulin since recognition of pregnancy – now PT 40 nocte and NR 22u TDS

Now 34/40 and AC 95th, EFW >99th

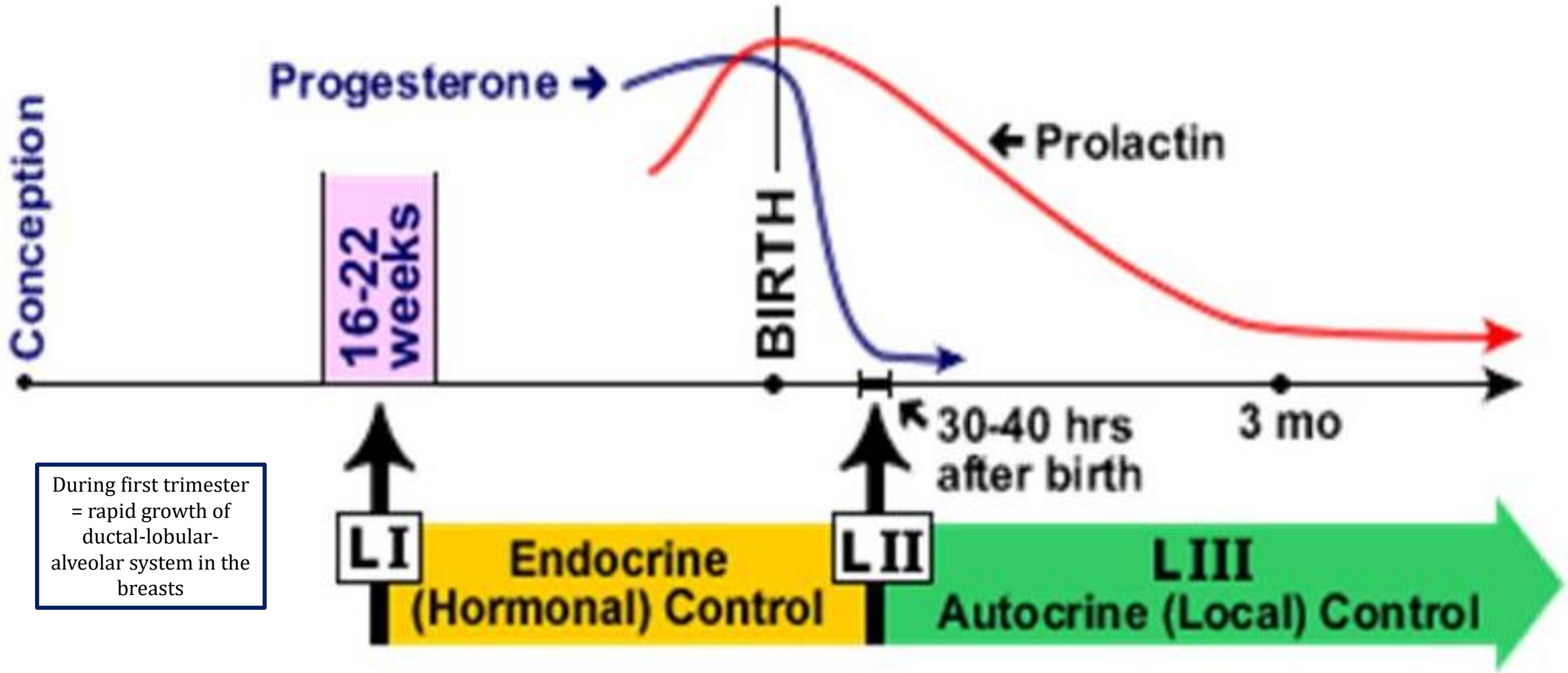
Obs suggesting elLSCS 38/40

Really keen to breastfeed!

CASE TWO

What breastfeeding difficulties might I encounter due to my type 2 diabetes?

Is there anything I can do now to help?



During first trimester = rapid growth of ductal-lobular-alveolar system in the breasts

Mammogenesis **Lactogenesis** **Galactopoesis**

Lactogenesis I = secretory initiation

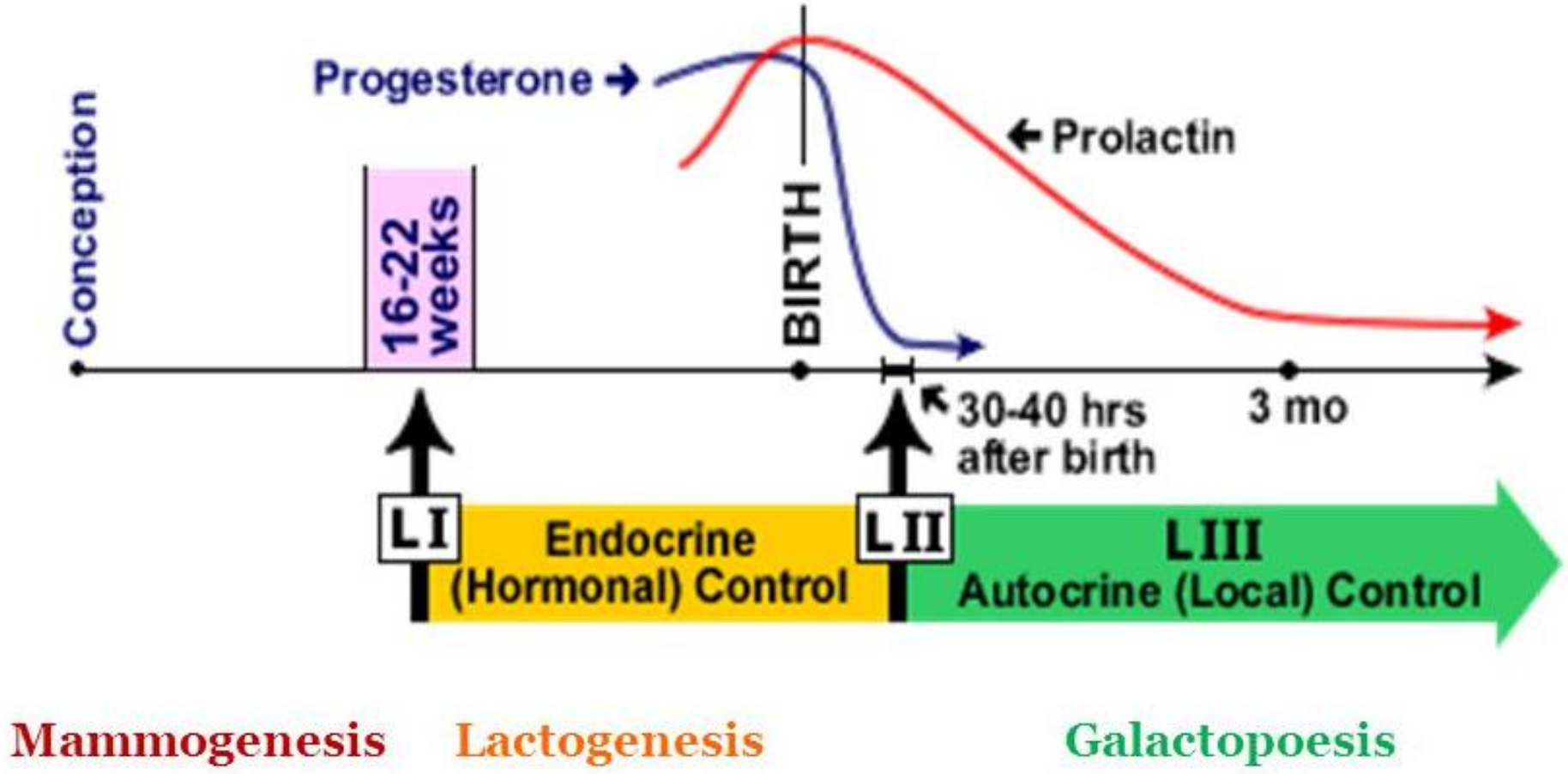
From 16-22 weeks

Endocrine control:
↑oestrogen
↑progesterone
↑prolactin
↑human placental lactogen

Initiation of milk synthesis

Alveoli differentiate into secretory cells, gene expression upregulated, production of small amounts of colostrum

However, high levels of placental progesterone inhibit copious milk production



Lactogenesis II = secretory activation

Endocrine control - initiated by fall of progesterone after delivery of the placenta

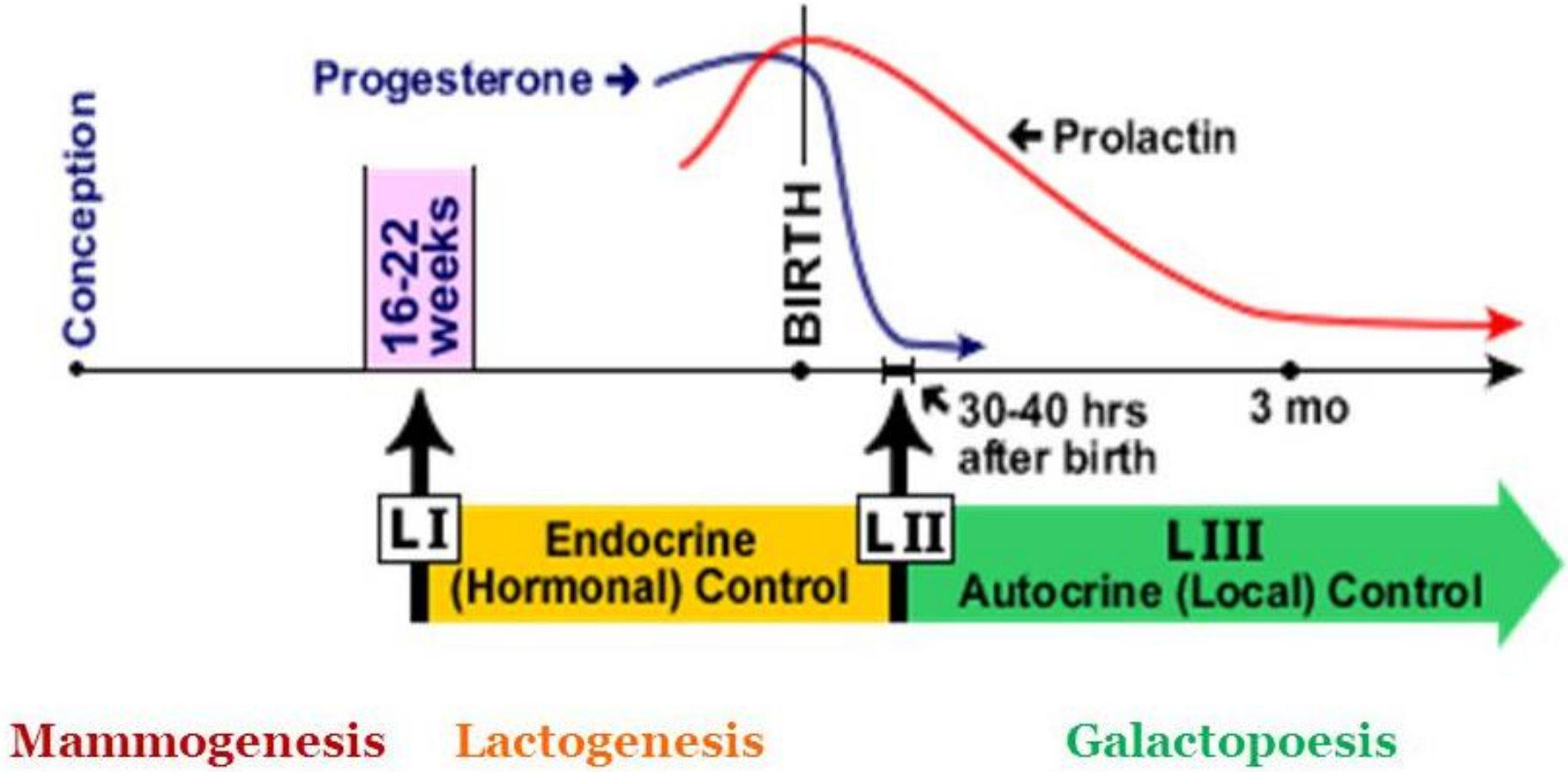
In *women with uncomplicated deliveries*, occurs 48-72h post-partum

Swelling of the breasts and onset of copious milk production ("milk coming in")

Lactogenesis III = established milk production

Under **autocrine (local) control** and driven by ongoing milk removal

Main lactational hormone PRL, with oxytocin responsible for 'let-down' reflex

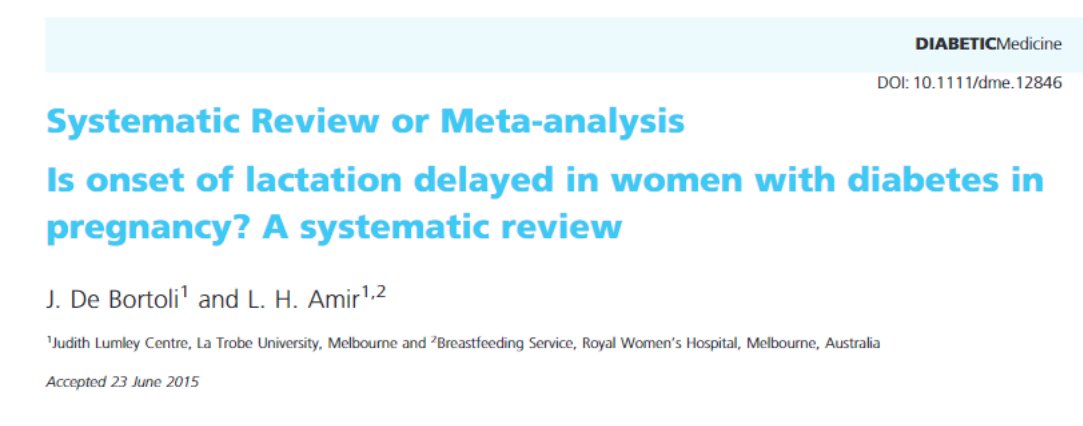


Delayed onset of lactogenesis II

- Defined as >72h after delivery
- Cues = breast swelling, milk leakage, change in milk physical appearance, breast fullness and pain
- **Maternal perception of OL** has been demonstrated to be a valid proxy for OL in comparison with the gold standard of test weighing – so this is used widely in studies
- Can also define biochemically – rise in milk citrate, lactose; fall in sodium, chloride and protein

Infant feeding patterns in first days of life shown to be a critical determinant of later feeding practises – studies consistently demonstrate strong association between DOL and shorter BF duration

Delayed onset of lactogenesis II in diabetes



DIABETICMedicine

DOI: 10.1111/dme.12846

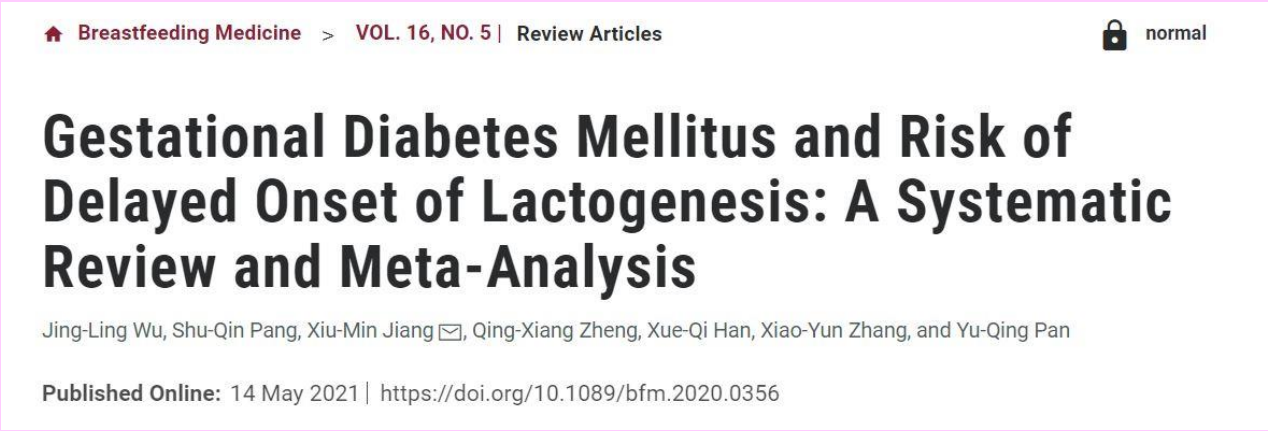
Systematic Review or Meta-analysis

Is onset of lactation delayed in women with diabetes in pregnancy? A systematic review

J. De Bortoli[1] and L. H. Amir[1,2]

[1]Judith Lumley Centre, La Trobe University, Melbourne and [2]Breastfeeding Service, Royal Women's Hospital, Melbourne, Australia

Accepted 23 June 2015



Breastfeeding Medicine > VOL. 16, NO. 5 | Review Articles

normal

Gestational Diabetes Mellitus and Risk of Delayed Onset of Lactogenesis: A Systematic Review and Meta-Analysis

Jing-Ling Wu, Shu-Qin Pang, Xiu-Min Jiang ✉, Qing-Xiang Zheng, Xue-Qi Han, Xiao-Yun Zhang, and Yu-Qing Pan

Published Online: 14 May 2021 | https://doi.org/10.1089/bfm.2020.0356

Two recent systematic reviews

- Amir et al, 2015 = 10 studies (7 T1DM, 3 GDM)
- Wu et al, 2021 = 11 studies, all GDM

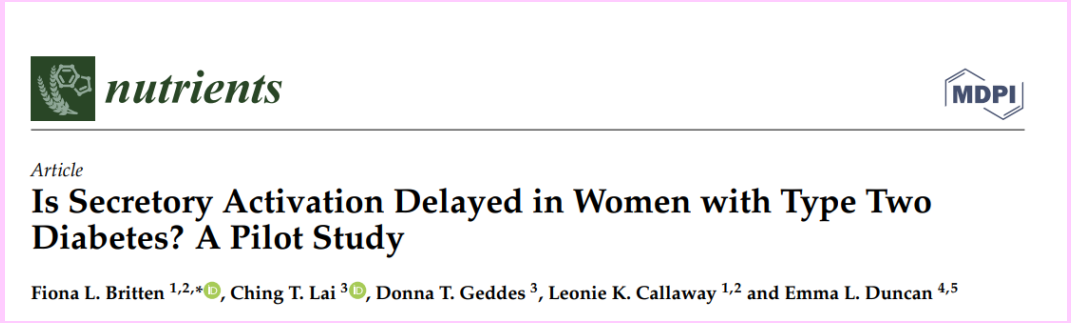
Consistent findings

1. Diabetes (T1DM and GDM) **clearly and consistently associated with DOL.**
2. Prevalence of DOL estimated at 35% for the GDM cohort.
3. DOL **more likely** in **primips, advanced age, insulin treatment, obesity, and worse metabolic control.**

CASE TWO

I've got **T2DM.** What about me?

Delayed onset of lactogenesis II in diabetes



nutrients

MDPI

Article

Is Secretory Activation Delayed in Women with Type Two Diabetes? A Pilot Study

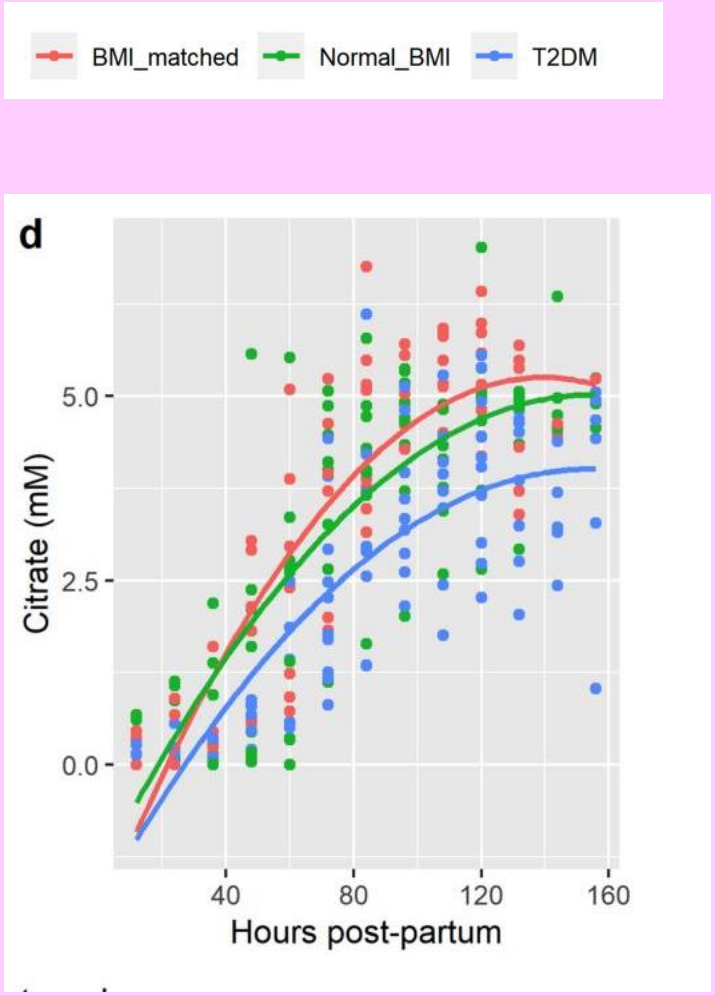
Fiona L. Britten [1,2,*], Ching T. Lai [3], Donna T. Geddes [3], Leonie K. Callaway [1,2] and Emma L. Duncan [4,5]

- n=14 with T2DM, mean BMI 30.6
- n=10 **BMI-matched** non-diabetic controls
- n=12 **normal-BMI** non-diabetic controls

- Lactogenesis onset via maternal perception, PLUS BM components measured twice daily for 5 days

Britten et al, *Nutrients*. 2002 Apr; 14(7): 1323.

Delayed onset of lactogenesis II in diabetes



Key findings =

- Citrate conc rose slower and plateaued at lower values in T2DM women compared with non-DM controls (both lean and BMI-matched) – suggests delayed onset of lactogenesis
- Larger insulin doses in T2DM were associated with later lactogenesis
- In addition to the presumed biological impact of the DM, T2DM was also associated with other clinical factors that might adversely impact on lactogenesis and breastfeeding: high rates of **neonatal hypoglycaemia** (10 of 14 babies), and high rates of **formula supplementation** (10 of 14 babies)
- Both T2DM women and BMI-matched non-diabetic controls were less likely to EBF at 4mo compared with normal-BMI controls

Britten et al, *Nutrients*. 2002 Apr; 14(7): 1323.

Delayed onset of lactogenesis II in diabetes

The diabetes physiology itself..

- ? Delayed substrate uptake (glucose, oxygen, LCFAs)
- **Insulin and insulin/ receptor interactions KEY to switch on genes for mammary differentiation and milk synthesis!** → insulin resistance or absence may impair milk production at lactocyte level

Clinical consequences of the diabetes…

- **Mothers with diabetes more likely to**
  - Have preterm delivery → less developed suckling reflexes, lower muscle tone, smaller mouths
  - Have Caesarean sections
  - Have babies with hypoglycaemia
  - Be separated from baby for NICU/ SCN
  - Be given early formula supplementation

… all independent RFs for delayed lactogenesis II

Delayed onset of lactogenesis II in diabetes – how can we help?

- Dearth of literature/ specific interventions

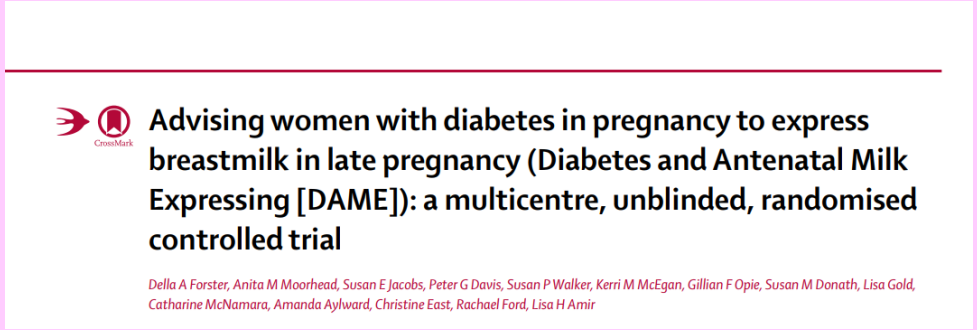
- Simple measures:
- Optimising glycaemic control during pregnancy and pre-delivery
- **Discuss <u>breastfeeding intention</u> and affirm it/ offer support**
- **Antenatal breastfeeding education** (ABA group classes etc)
- **Antenatal expression of colostrum**
- Early skin-to-skin, opportunity to BF within 30-60min
- Avoid mother/baby separation unless medically indicated
- If mother in ICU, breastmilk expression immediately following stabilisation
- Early LC involvement and support

Antenatal expression and the DAME STUDY

- Manual expression of colostrum in last few weeks of pregnancy – allows storage of small amounts of colostrum to be given to infant prior to established milk supply (lactogenesis II) at day 2-3
- For mothers with diabetes – stored colostrum can be used to correct mild neonatal hypoglycaemia
- **Women typically advised to "check with antenatal care provider first"**
- From 36 weeks – 3-5 minutes of hand expressing each breast, 2-3 times per day
- Collect into medicine cup, aspirate into syringe, cap syringe, label, and freeze within 24h of expressing
- Small amounts – few mL!
- 25% unable to express antenatally – not a harbinger of low supply post-partum
- **The Royal Women's Hospital (Melbourne, Aus)** has good online instruction handout for patients

Antenatal expression and the DAME STUDY

- Safety considerations – theoretical risk of oxytocin surge, ↑ uterine activity and promotion of premature labour?
- 2 small early/ pilot studies 2011-2012 showed increased risk of early delivery and increased NICU admissions, some calls for practise to be halted awaiting further research
- Definitive trial = **DAME study, Lancet 2017**
  - Six hospitals in Victoria
  - Women with GDM or DIP, low-risk singleton preg, 34-37 weeks, n=635
  - Randomised to BD expression from 36/40 (n=319) or standard care (n=316)
  - Expressing group – median 20 episodes, 5.5mL collected
  - **No diff** in NICU admissions (RR for expressing group 1.06, 95% CI 0.66-1.46)
  - **No diff** in mean gestational age between groups
  - Moderate association between allocation to expressing group and receipt of exclusive breastmilk to 24h (RR for expressing group 1.15, 95% CI 1.02 – 1.28)
- Now considered a safe and accepted practise



Advising women with diabetes in pregnancy to express breastmilk in late pregnancy (Diabetes and Antenatal Milk Expressing [DAME]): a multicentre, unblinded, randomised controlled trial

Della A Forster, Anita M Moorhead, Susan E Jacobs, Peter G Davis, Susan P Walker, Kerri M McEgan, Gillian F Opie, Susan M Donath, Lisa Gold, Catharine McNamara, Amanda Aylward, Christine East, Rachael Ford, Lisa H Amir

"There is no harm in advising women with diabetes in pregnancy at low risk of complications to express breastmilk from 36 weeks' gestation, and some evidence of benefit"

NOT advisable if: imminent PTL or high risk of same, cervical incompetence or cerclage, hx of APH or placenta previa. STOP if increased Braxton-Hicks or similar

Forster et al. *Lancet*, 2017: 389:10085, p2204-2213.

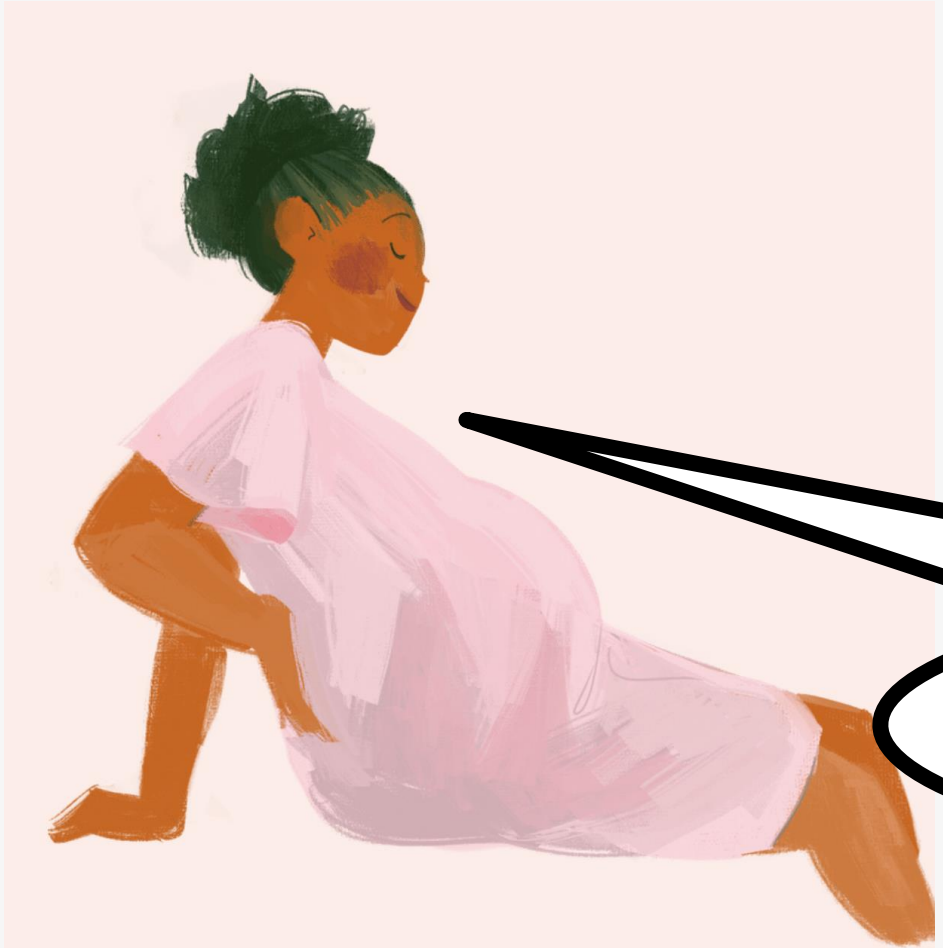
CASE TWO

Zara has had her baby via elLSCS. Early skin to skin was a priority.

He had mild hypoglycaemia and she was able to supplement with her expressed colostrum.

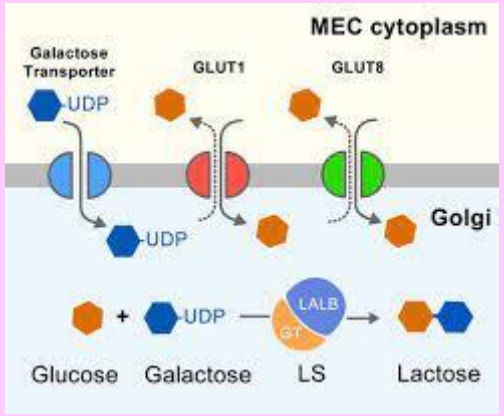
She is 4/7 postpartum and her milk has come in. She is highly motivated to BF.

She has resumed metformin, but her fasting BSLs on day 2 PP were 10-12; so insulin has been reintroduced (PT 10 nocte).



Will my milk be full of sugar?
What about my insulin – does that get into milk, and is it safe for baby?

"Will my milk be full of sugar?"



- Passive transport of glucose into the mammary gland by GLUT1
- Majority of the glucose **used to synthesise lactose** (= major carbohydrate constituent of breastmilk and main determinant of its volume)
- Once lactation established, most studies suggest that lactose content of breastmilk samples from women with DM is similar to that of controls

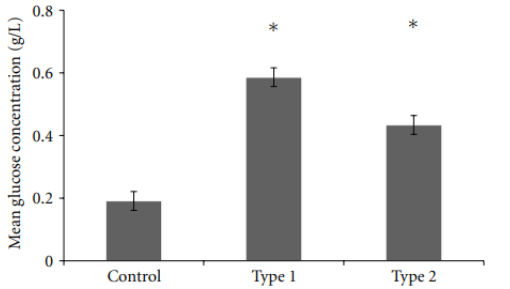


FIGURE 4: Mean glucose content of milk in each group. *indicates significant difference ($P < 0.05$) compared to control mothers.

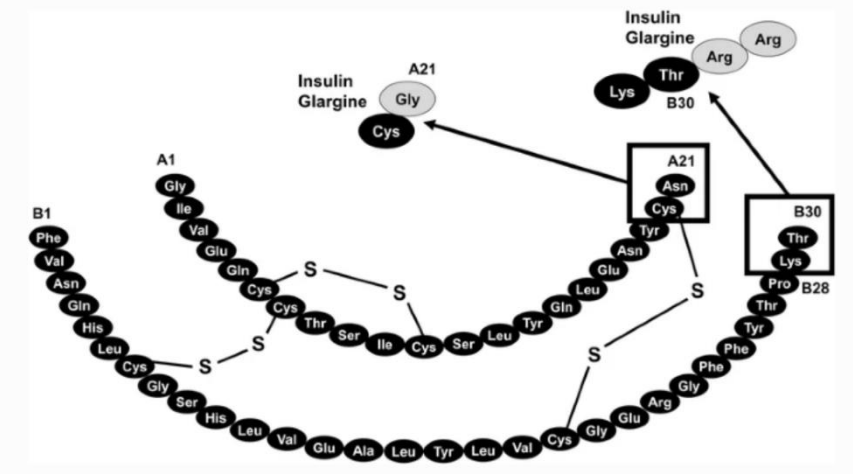
- Breastmilk does contain a very small amount of free glucose, and studies suggest this amount is likely to be higher and more variable in mothers with T1 and T2DM than control women
- Experimentally induced hyperglycaemia in DM does elevate BM glucose (lag time 40-90 minutes)
- **However, glucose concentrations about 100x lower than lactose concentrations!**
- **Glucose accounts for 0.4% of the total energy content of breastmilk (compared with 40% for lactose) so clinical significance of this variation is dubious**

Note that the typical lactose concentration is 75g/L!

Whitmore et al, Int J Endocrinology. 2012: 296368.

"Will my insulin enter my breastmilk?"

Exogenous insulin use is compatible with breastfeeding; insulin is a normal component of human milk and is not expected to be orally bioavailable to the infant [33,35].



- Insulin known to be present in both colostrum and mature milk, in both diabetic and control women
- **Concentrations close to that of serum,** so probably actively transported into milk!

- Insulin typically thought to have no biological action when orally ingested, BUT
- insulin receptors ARE present on the intestinal epithelium of other large mammals → milk-borne insulin helps with intestinal maturation [1]
- ? a similar role in humans – enteral insulin given to preterm infants enhanced GI function in one study [2]
- ? also roles for breastmilk insulin in gut microbiome development, and development of healthy gut immune tolerance [3]

- If so - artificial recombinant human insulins typically only 1-3 aa different to human insulins

[1] Whitmore et al, *Int J Endocrinology.* 2012: 296368.
[2] Shulman RJ. *Arch Dis Child Fetal Neonatal Ed.* 2002(2):131-133.
[3] Lemas et al, *Am J Clin Nutr.* 2016(103):5.

CASE THREE

Martine, 29F

G1P1
2 weeks post-partum

Background of PCOS. Oligomenorrhoea pre-preg, 3-4 cycles a year, required letrozole for OI to conceive

BMI 37

Referred to you with suspected low supply – ++unsettled baby, still well below birthweight

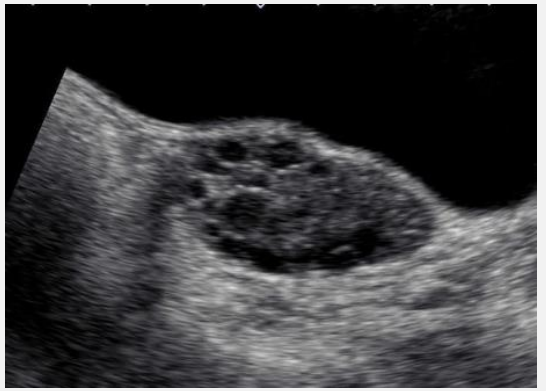
Could this be because of my PCOS?

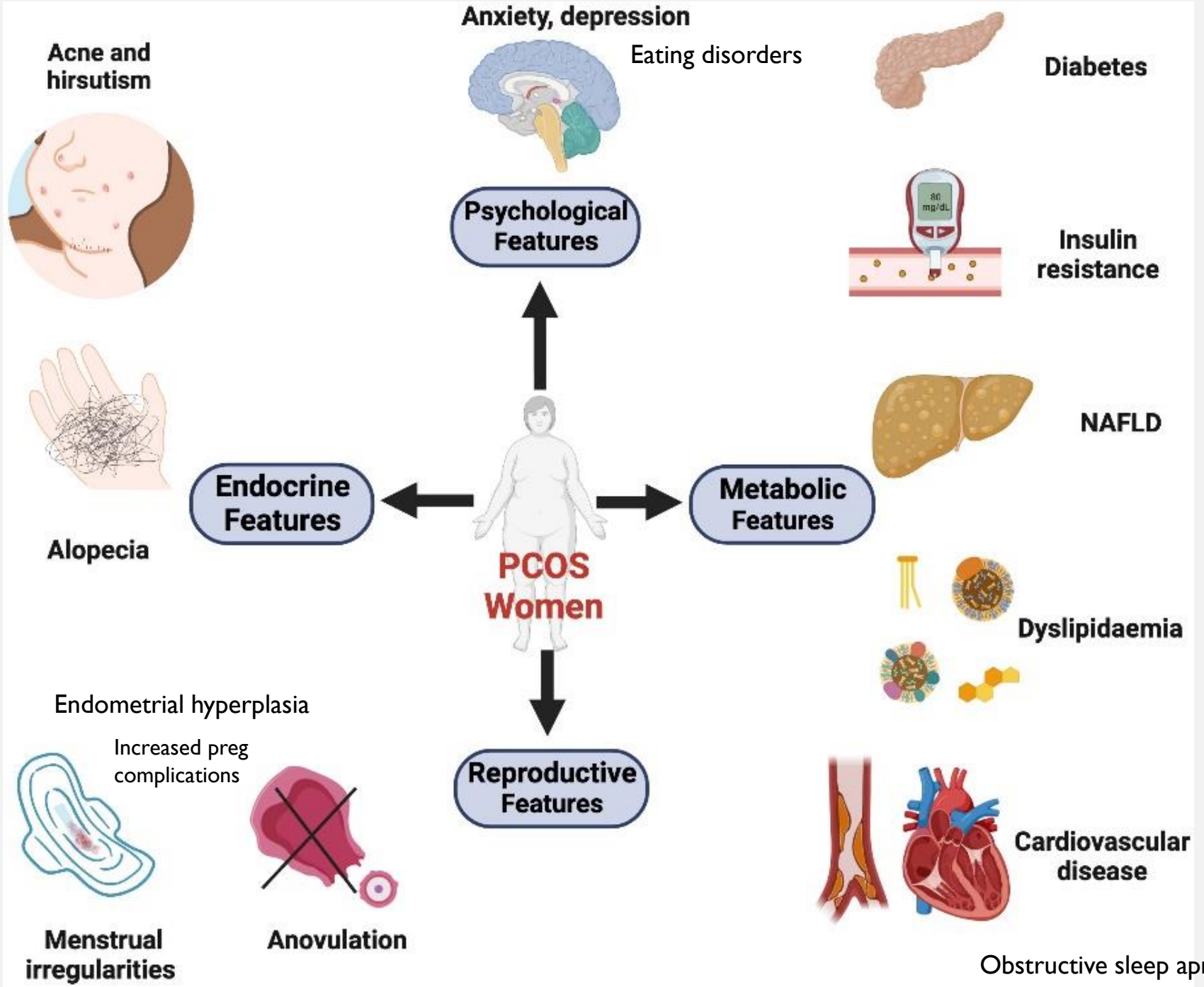
PCOS: A RECAP

- 5-18% of women – commonest endocrine disorder amongst women of reproductive age

- **Rotterdam criteria** – 2 of 3 required for diagnosis (in adults):
- oligo- or amenorrhoea (<21 or >35 day cycles, or <8 cycles per year)
- hyperandrogenism (clinical – hirsutism, acne, scalp hair loss; OR biochemical – check total Te, SHBG, calc FAI)
- polycystic ovarian morphology on ultrasound (20 or more follicles on either ovary, or OV of 10mL or above)*

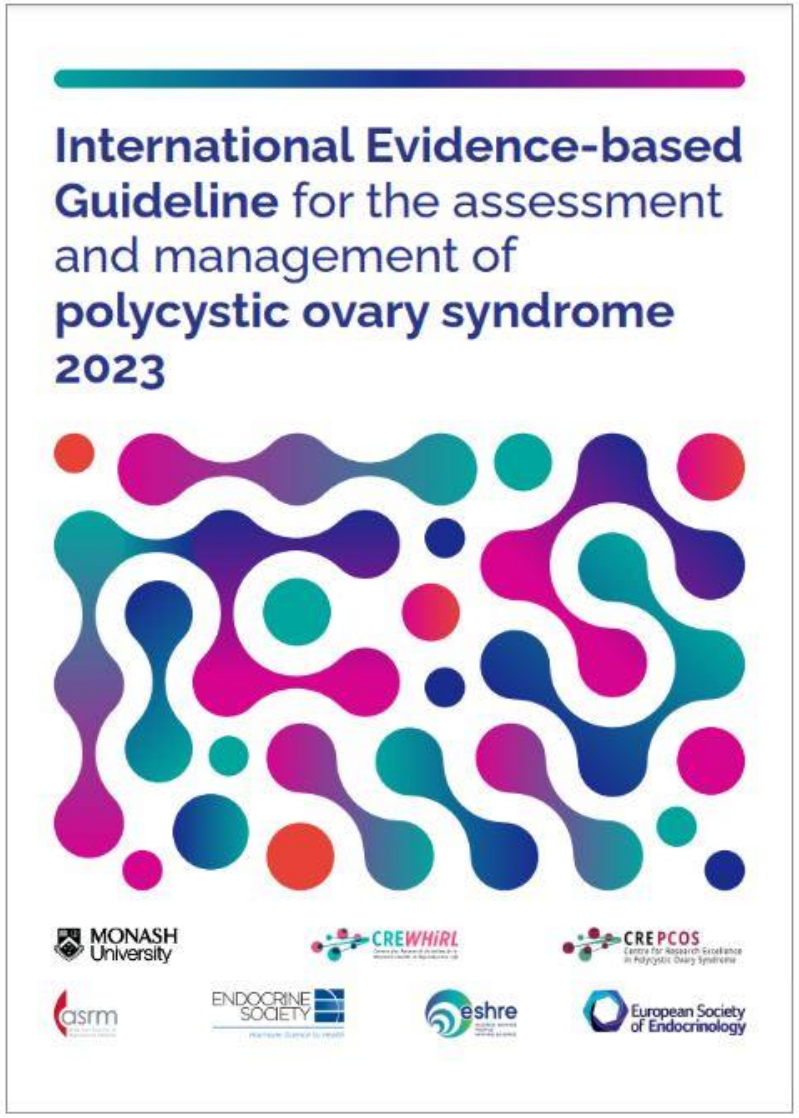
*or elevated AMH, if USS not performed





Pro tips:

- Confusing name, complex pathophysiology and lots of "myths" (and a big social media presence!)
- *Education* is a large part
- Patient priorities vary hugely across the lifespan, and between individuals. Long-term chronic condition needing good therapeutic relationship
- Big overlap with obesity and weight management
- **Monash 2023 Evidence Based Guidelines** should be go-to


International Evidence-based Guideline for the assessment and management of polycystic ovary syndrome 2023
MONASH University
CREWHiRL
CRE PCOS
Centre for Research Excellence in Polycystic Ovary Syndrome
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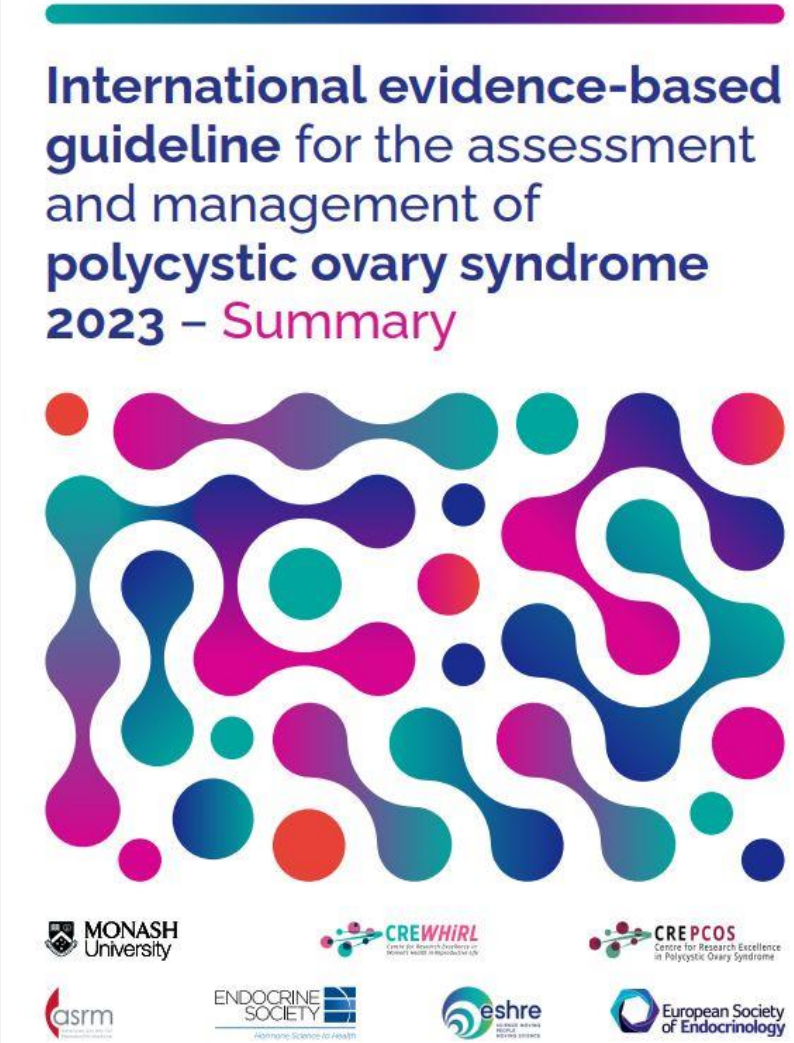
International evidence-based guideline for the assessment and management of polycystic ovary syndrome 2023 – Summary
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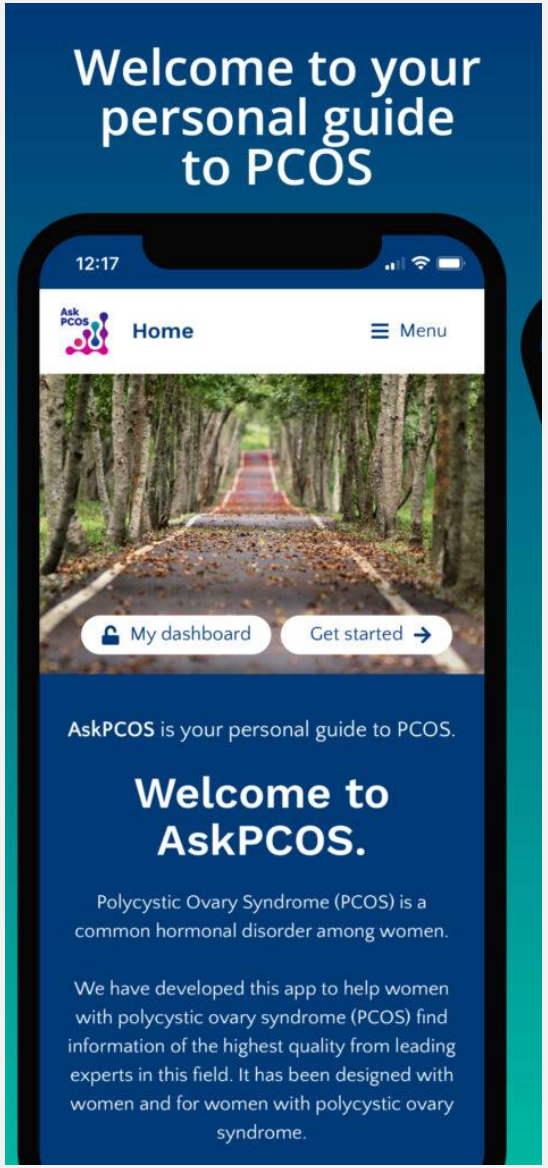

Welcome to your personal guide to PCOS
12:17
Ask PCOS
Home
Menu
My dashboard
Get started
AskPCOS is your personal guide to PCOS.
Welcome to AskPCOS.
Polycystic Ovary Syndrome (PCOS) is a common hormonal disorder among women.
We have developed this app to help women with polycystic ovary syndrome (PCOS) find information of the highest quality from leading experts in this field. It has been designed with women and for women with polycystic ovary syndrome.

PCOS AND BREASTFEEDING

- Small case-control studies (and individual case studies) suggesting reduced breastfeeding success in PCOS compared with controls [1, 2, 3]

- Our work in Aus community-based cohort (approx. 13000 live births) suggested
- **marginal differences** in BF duration in PCOS vs. non-PCOS women (median complete duration 7 vs 9 months)
- no sig difference in adjusted odds of initiation of BF, nor odds of BF beyond 6mo; according to PCOS status
- main independent predictor of BF initiation and duration was **maternal BMI, moreso than any specific maternal metabolic condition** [4]

[1, 2, 3] Marasco et al. *J Hum Lact* 2000; 86(2):404-411; Vanky et al. *Acta Obstet Gynecol Scand* 2008; 87(5):531-535; and McGuire and Rowan. *Breastfeeding Rev* 2015 Nov; 23(3): 29-32.
[4] Rassie et al. *Acta Obstet Gynecol Scand* 2024;00:1-14.

MECHANISMS?

- **Obesity!** Big overlap with PCOS - but also other disease-specific factors?

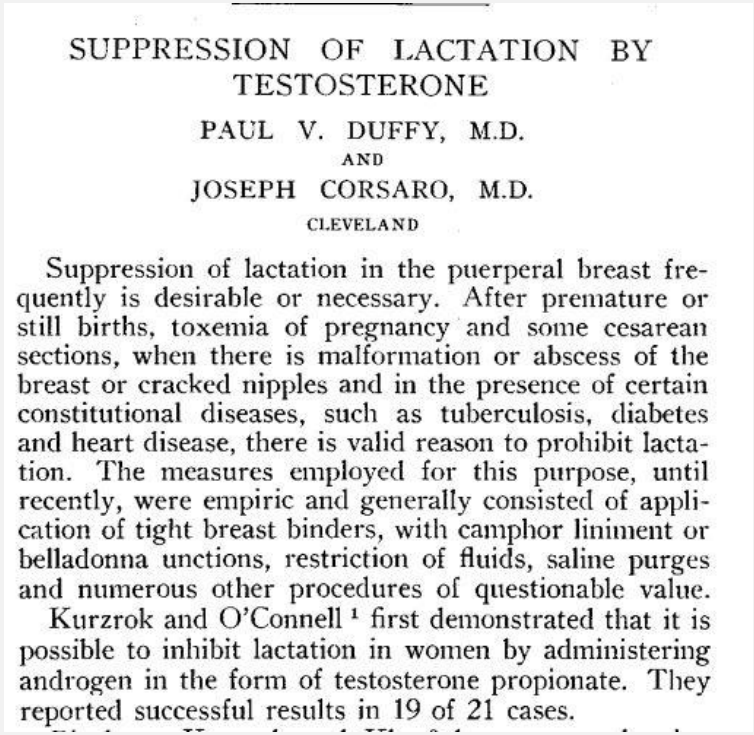
1. Insulin resistance

- Insulin important for milk synthesis (switches on key lactation genes)

2. Androgen effect

- Testosterone given historically to shut down lactation!
- One study (in a general pop) showing maternal androgen levels at mid-pregnancy negatively associated with breastfeeding at 3 and 6mo[1], and another (in a PCOS pop) showing maternal DHEAS at week 32 and 36 negatively associated with breastfeeding at 1 and 3 mo [2]

3. Link to breast hypoplasia/ insufficient glandular tissue?



SUPPRESSION OF LACTATION BY TESTOSTERONE

PAUL V. DUFFY, M.D.
AND
JOSEPH CORSARO, M.D.
CLEVELAND

Suppression of lactation in the puerperal breast frequently is desirable or necessary. After premature or still births, toxemia of pregnancy and some cesarean sections, when there is malformation or abscess of the breast or cracked nipples and in the presence of certain constitutional diseases, such as tuberculosis, diabetes and heart disease, there is valid reason to prohibit lactation. The measures employed for this purpose, until recently, were empiric and generally consisted of application of tight breast binders, with camphor liniment or belladonna unctions, restriction of fluids, saline purges and numerous other procedures of questionable value.

Kurzrok and O'Connell [1] first demonstrated that it is possible to inhibit lactation in women by administering androgen in the form of testosterone propionate. They reported successful results in 19 of 21 cases.

[1] Carlsen et al. Acta Obstet Gynecol Scand. 2010;89(1): 87-94.
[2] Vanky et al. Acta Obstet Gynecol Scand. 2008; 87: 531-535.

BREAST HYPOPLASIA/ INSUFFICIENT GLANDULAR TISSUE

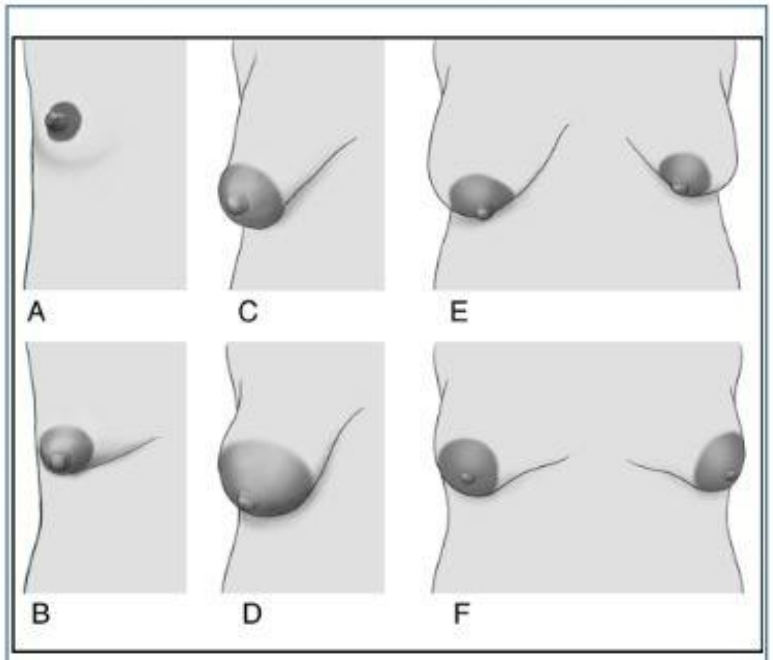


Figure 1. Mammary Hypoplasia Variations.
A) Incomplete development before puberty; B) Poorly developed upper portion, scant lower tissue; C) Tubular with bulbous areola; D) Long, bowed to outside, with extra-large areola; E) Classic wide spaced and uneven; and F) Wide spaced with scant tissue.

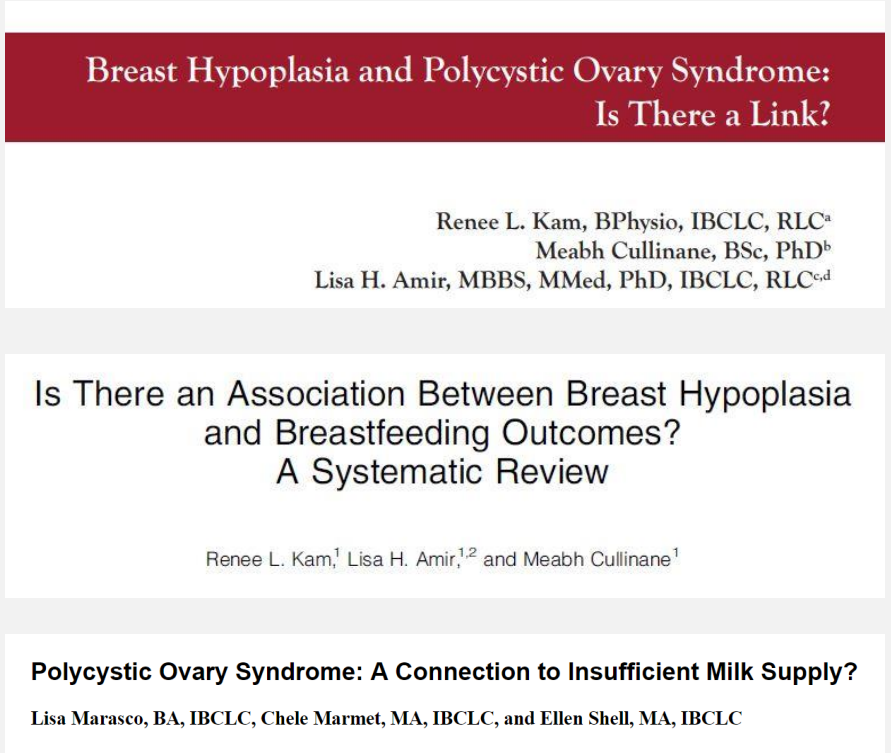
- Research suggests little correlation between breast size and milk production ability
- However, successful lactation does require adequate **glandular tissue**, which relies on ductal proliferation in puberty and then in pregnancy

- Mammary hypoplasia = lack of glandular tissue
- Textbooks: tubular shaped, droopy, or asymmetrical breasts; wide intra-mammary width (>3.8cm); little or no breast growth in pregnancy; minimal breast tissue in inferior quadrants

- In some women, breasts like this do seem to predict primary lactation insufficiency (and early cessation of EBF despite best efforts)
- No agreed definition/ diagnostic criteria, and unclear which factors may make the condition more or less relevant to milk production ability

Arbour et al. J Midwifery Womens Health 2013; 58:457461.

BREAST HYPOPLASIA/ INSUFFICIENT GLANDULAR TISSUE



Breast Hypoplasia and Polycystic Ovary Syndrome: Is There a Link?

Renee L. Kam, BPhysio, IBCLC, RLC[a]
Meabh Cullinane, BSc, PhD[b]
Lisa H. Amir, MBBS, MMed, PhD, IBCLC, RLC[c,d]

Is There an Association Between Breast Hypoplasia and Breastfeeding Outcomes? A Systematic Review

Renee L. Kam,[1] Lisa H. Amir,[1,2] and Meabh Cullinane[1]

Polycystic Ovary Syndrome: A Connection to Insufficient Milk Supply?

Lisa Marasco, BA, IBCLC, Chele Marmet, MA, IBCLC, and Ellen Shell, MA, IBCLC

Link between **PCOS** and breast hypoplasia/ IGT is well-described at level of case reports and case series; and in some historical studies examining soft tissue radiography

Theoretical mechanisms:

- **Lower progesterone, and/ or pre-pubertal obesity** → impaired glandular tissue development in puberty
- Impaired **breast size increment** across pregnancy
- **Insulin resistance** (insulin/ receptor interaction essential to switch on genes for breast development)
- Inhibitory effect of **androgens** on mammary gland development and lactation

Kam et al, Clinical Lactation, 2021, 12(4).
Kam et al, Breastfeeding Med 2021; 16(8).
Marasco et al, J Hum Lact 2001; 16(2).

BREAST HYPOPLASIA/ INSUFFICIENT GLANDULAR TISSUE

Management?

- **Good antenatal history-taking:**
- Hormonal history – known PCOS, DM, obesity? Subfertility?
- Surgery or injury to breasts or chest (may have had surgery to correct hypoplastic breasts)
- Breast changes during pregnancy; weight changes during pregnancy
- Breast exam – widely spaced, tubular, asymmetrical?

Acknowledge **BF priorities** and **psychosocial context/ supports**

If primary insufficient milk supply does occur, strategies as per usual guidelines (including galactogogue therapy).

Infant Feeding - Management of Low Breast Milk Supply Guideline

the women's
the royal women's hospital

BREASTFEEDING MEDICINE
Volume 13, Number 5, 2018

DOI: 10.1089/bfm.2018.29092.wjb

ABM Protocol

ABM Clinical Protocol #9: Use of Galactogogues in Initiating or Augmenting Maternal Milk Production, Second Revision 2018

Wendy Brodribb and the Academy of Breastfeeding Medicine

CASE THREE

What about metformin? Someone on Reddit said that it might help supply in PCOS.

IS THERE A ROLE FOR METFORMIN IN AUGMENTING MILK SUPPLY IN PCOS?

Journal of Human Lactation
Volume 35, Issue 2, May 2019, Pages 261-271

https://doi.org/10.1177/0890334418819465

Clinical Practice

Feasibility and Acceptability of Metformin to Augment Low Milk Supply: A Pilot Randomized Controlled Trial

Laurie Nommsen-Rivers, PhD, RD, IBCLC [1], Amy Thompson, MD [1], Sarah Riddle, MD, IBCLC [1,2], Laura Ward, MD, IBCLC [1,2], Erin Wagner, MS [1], and Eileen King, PhD [1,2]

Small pilot RCT examining the feasibility of metformin to treat low milk supply

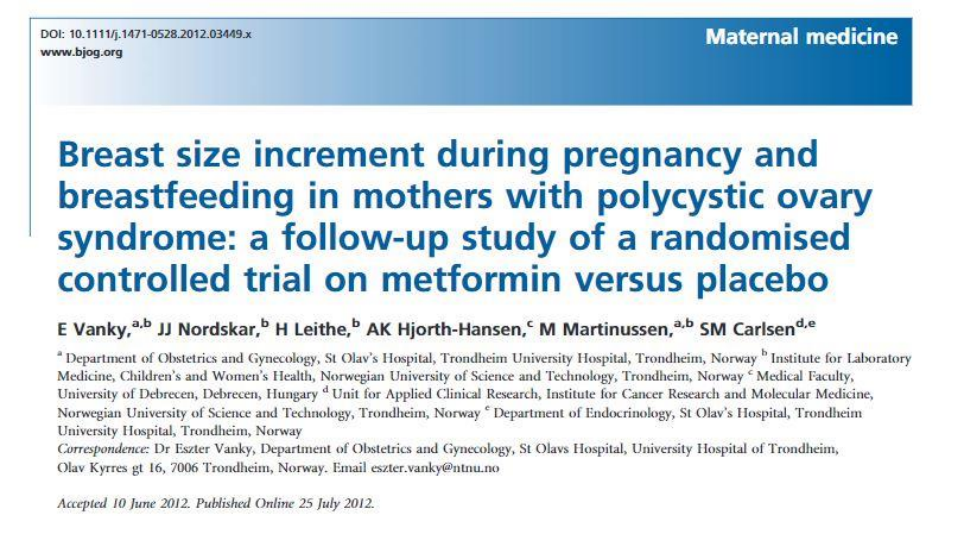
Participants "insulin resistant": elevated fasting glucose, hx GDM, PCOS or central obesity

N=10 metformin
N=5 placebo
Commenced at a median of 36 days post-partum

Median peak change in milk supply per 24h was **+22ml** for metformin completers vs **-58ml** for placebo and non-completers – trend, but not SS

No participants perceived metformin as worthwhile
Feasibility concerns about upscaling to larger trial

IS THERE A ROLE FOR METFORMIN IN AUGMENTING MILK SUPPLY IN PCOS?



DOI: 10.1111/j.1471-0528.2012.03449.x
www.bjog.org

Maternal medicine

Breast size increment during pregnancy and breastfeeding in mothers with polycystic ovary syndrome: a follow-up study of a randomised controlled trial on metformin versus placebo

E Vanky,[a,b] JJ Nordskar,[b] H Leithe,[b] AK Hjorth-Hansen,[c] M Martinussen,[a,b] SM Carlsen[d,e]

[a] Department of Obstetrics and Gynecology, St Olav's Hospital, Trondheim University Hospital, Trondheim, Norway [b] Institute for Laboratory Medicine, Children's and Women's Health, Norwegian University of Science and Technology, Trondheim, Norway [c] Medical Faculty, University of Debrecen, Debrecen, Hungary [d] Unit for Applied Clinical Research, Institute for Cancer Research and Molecular Medicine, Norwegian University of Science and Technology, Trondheim, Norway [e] Department of Endocrinology, St Olav's Hospital, Trondheim University Hospital, Trondheim, Norway

Correspondence: Dr Eszter Vanky, Department of Obstetrics and Gynecology, St Olavs Hospital, University Hospital of Trondheim, Olav Kyrres gt 16, 7006 Trondheim, Norway. Email eszter.vanky@ntnu.no

Accepted 10 June 2012. Published Online 25 July 2012.

Followup of the PregMet study (n=240), which looked at **metformin vs placebo in pregnant women with PCOS**

MF 2g/ day (or placebo) taken all pregnancy and stopped at delivery

N=186 responded to a questionnaire at 1 year post-partum

<u>Key positive findings</u>

Women reporting **no breast size increment** across pregnancy
- had shorter BF duration (exclusive and partial)
- had worse metabolic health (higher BP, more obese, higher first trimester insulin and glucose levels)

BUT

NO differences in duration of exclusive or partial BF

NO differences in breast size increment across pregnancy

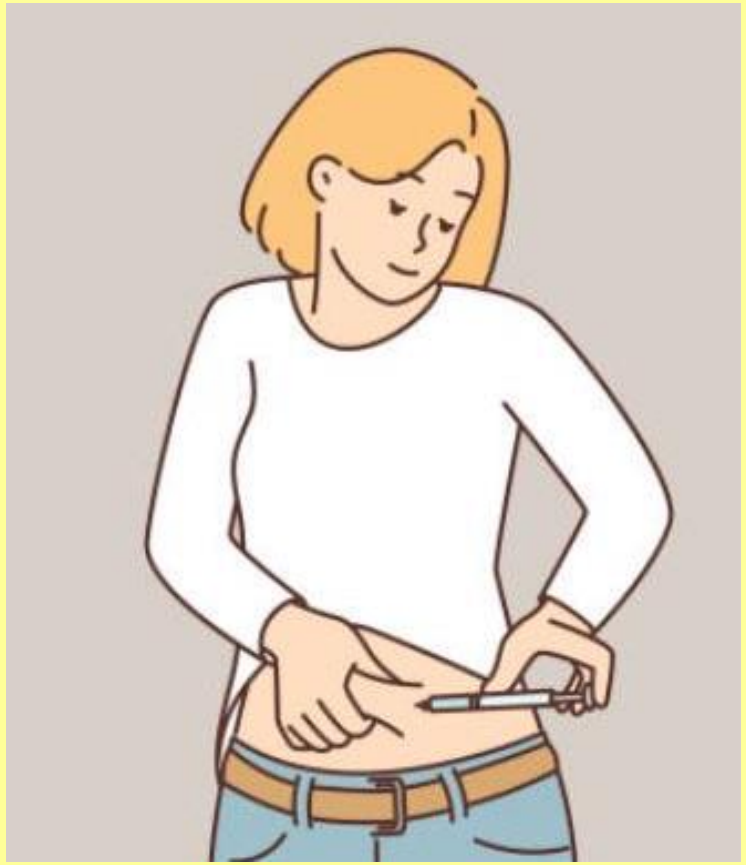
….according to <u>MF vs placebo status</u>.

IS THERE A ROLE FOR METFORMIN IN AUGMENTING MILK SUPPLY IN PCOS?

- Makes **mechanistic sense in the setting of insulin resistance, but currently insufficient evidence to support its use for the primary indication of augmenting milk** supply

- Patients who may be taking it for diabetes or PCOS may safely continue it during lactation, and could be informed that it may theoretically regulate the hormonal environment in a way that supports lactation

CASE FOUR



Alice, 29F

T1DM diagnosed aged 7

Pump in childhood, currently on MDI with Optisulin and NovoRapid
Well-controlled, engaged with endocrinologist and CDE

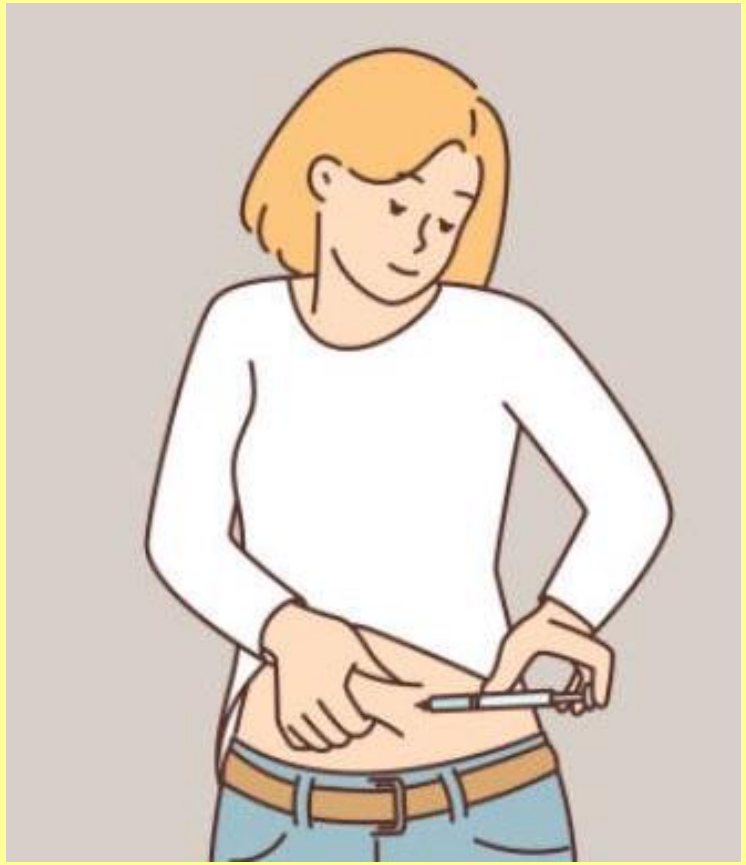
Preconception HbA1c 7.1% (ADIPS suggest <6.5% if achievable without hypos)
Using Freestyle Libre

Weight 60kg

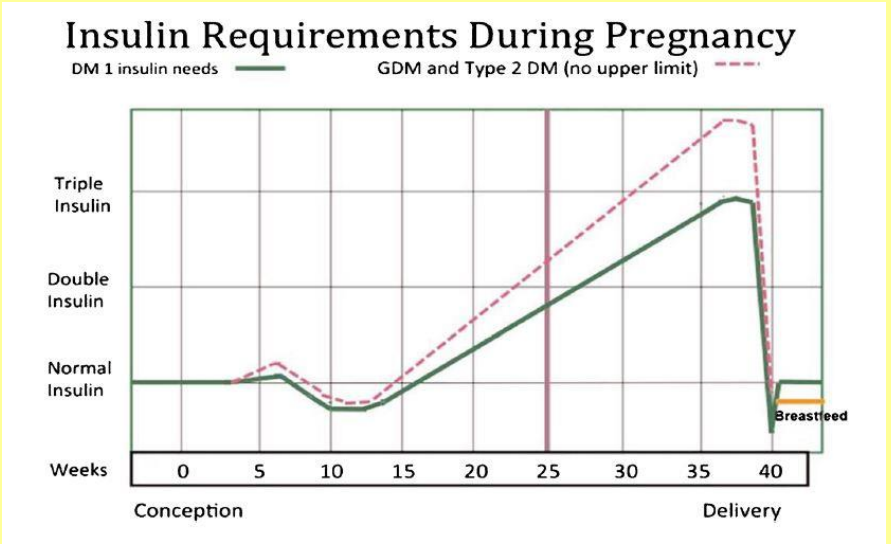
Pre-pregnancy TDD (total daily dose) of **30 units** approx

Basal = **15u** Optisulin mane
Bolus = **15u** Novorapid across the day
roughly 5 units TDS as per meal size (CHO ratio approx. 1:10)

CASE FOUR



Final antenatal endocrinology visit at 37/40:



Lots more insulin!

TDD 30u → **75u**

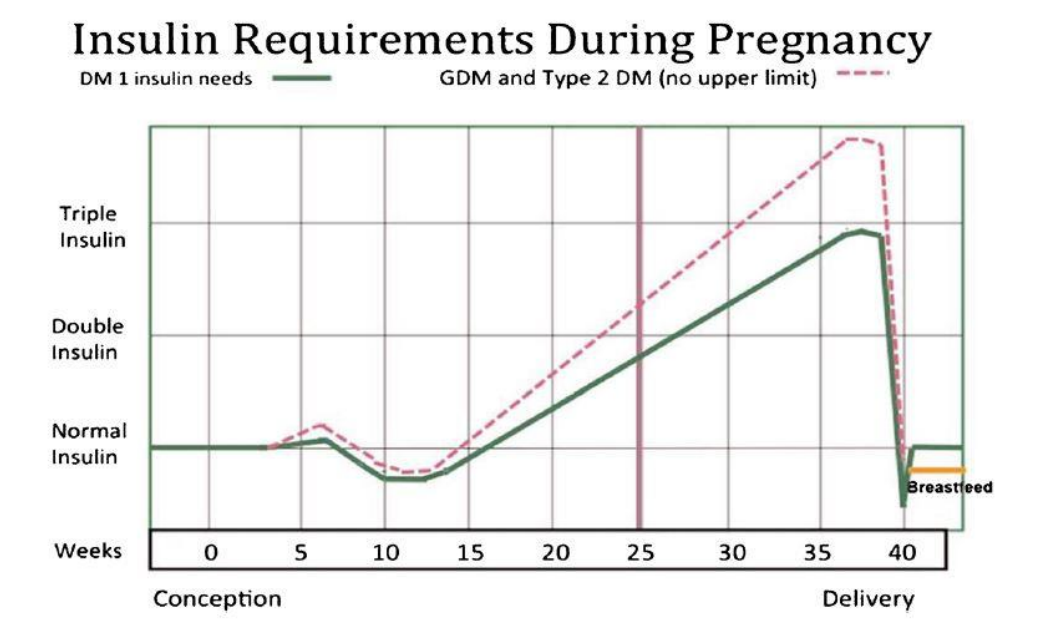
- 15u → **25u** Optisulin mane
- 15u → **50u** Novorapid across the day

(carb ratio approx. 1:3 at BF, 1:4 at lunch and dinner; 12-18 units per meal)

CASE FOUR

I'm keen to breastfeed.
What do I need to look out for in the first few days as I establish that?
My midwife mentioned hypos at the breast.

DURING THE HOSPITAL STAY



- Insulin requirements fall immediately after the delivery of the placenta – may be 30-50% lower than **pre-pregnancy** doses

- Should have a delivery plan and a post-partum plan provided by endo team
- Hourly BSLs in hospital until the first meal
- NO bolus insulin with the first meal, as tendency to hypo

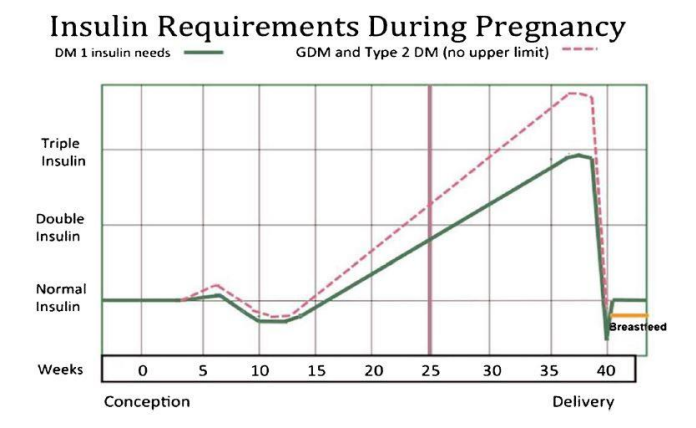
- **Prepare for BSLs to be a moving target for the first 3-5 days post-partum**
- **Often need contact with an inpatient endo team daily, if not more frequently**

- RELAX glycaemic targets!
- ADIPS BSL targets during pregnancy = <5.3 fasting, <6.8 2h PP
- Now suggest **5-10 mmol/ L across the board** as perfectly acceptable
- Have plenty of hypo snacks on hand

THE FIRST 6 WEEKS

- A tough ship to steer!
- Insulin requirements changing
- Need to maintain diet with sufficient carb intake to support lactation, maintain blood glucose levels and prevent ketoacidosis
- Frequent self-monitoring and adjustments required WHILST coping with demands of new motherhood, broken sleep etc
- Episodes of mild hypo- and hyper- glycaemia are inevitable

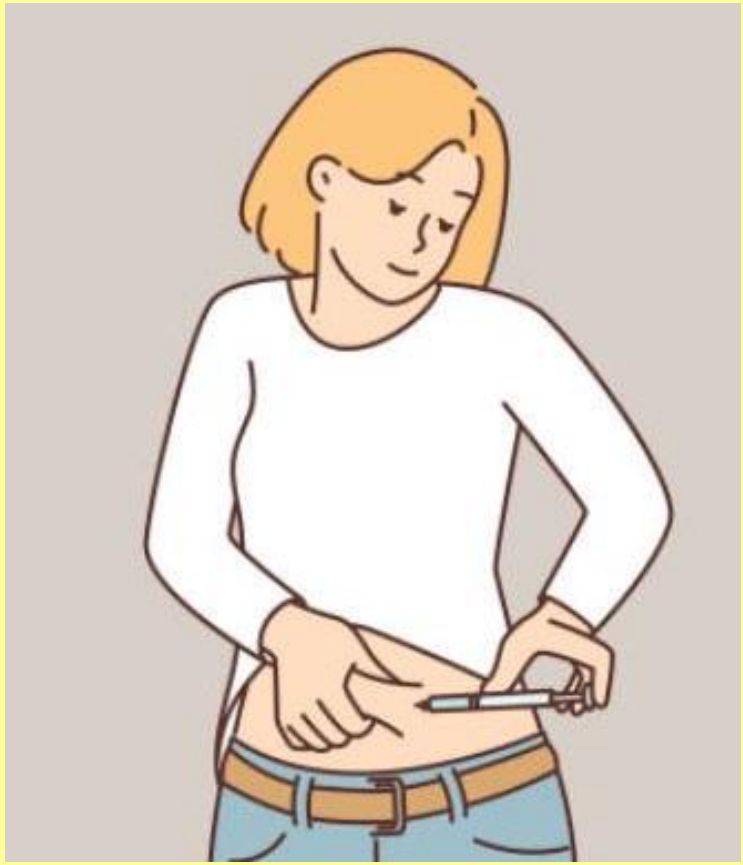
THE FIRST 6 WEEKS



- Few studies on how BF impacts T1DM management in the post partum
- Literature suggests insulin requirements in EBF women with T1DM may remain on average <u>20% lower than pre-pregnancy</u> from months 1-4 PP, but with wide individual variation
- IOM recommends **minimum of 210g of carbohydrate per day** (and at least 1800kcal/ day) for BF women

- Breastfeeding *per se* does not usually seem to induce acute hypoglycaemia (in contrary to some historical advice)
- ROUTINE consumption of carbohydrates during overnight feeds to prevent hypos is probably not necessary in the CGM era; on the condition that overall carb intake is adequate and insulin doses have been properly reduced

CASE FOUR



Alice returns to see us at 8 weeks post-partum.

	Pre-pregnancy	End of pregnancy	Breastfeeding
Basal insulin (Optisulin)	15u	25u	12u
Prandial insulin (Novorapid)	5u TDS = 15u	12-18u TDS = 50u	4u TDS = 12u
Total daily dose	30u	75u	24u

Libre – average glucose 8-9mmol/L, 3-4 mild hypos/ week

Watches BSL on her phone during long feeds, but no need to "prophylactically" consume CHO

Anticipate gradual return to pre-pregnancy doses over the next 2-3 mo

KEY POINTS

- Lactation is consistently associated with improved maternal metabolic outcomes – but does this reflect the **reset** hypothesis or the **preset** hypothesis?

- Delayed onset of lactogenesis common in women with diabetes in pregnancy
- Antenatal colostrum expression safe and may be helpful, but is an individual decision

- PCOS and breastfeeding under-researched; big overlap with obesity
- Link to IGT is acknowledged (and interesting!), although mainly anecdotal/ case studies
- Role of metformin unclear

- Type 1 diabetes in the postpartum is characterised by insulin sensitivity, and relaxation of the strict glycaemic targets of pregnancy. Specialist support is vital