Determining the Optimal Timing of Delivery for Women with Gestational Diabetes

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Gestational Diabetes (GDM)

- GDM – ‘any degree of glucose intolerance with onset *or first recognition* during pregnancy’
- Clinical controversies surround who to screen for GDM (i.e. targeted vs. universal screening) and what diagnostic criteria (i.e. Canadian Diabetes Association criteria vs. International Association of Diabetes and Pregnancy Study Groups criteria) to use
- Once diagnosed, GDM may be treated with lifestyle interventions, oral hypoglycemic agents or insulin depending on the severity of the condition

Benhalima 2015 Best Pract Res Clin Obstet Gynaecol
Berger 2002 JOGC
Thompson 2013 Can J Diab

GDM and Fetal Growth

- As fetuses exposed to GDM are exposed to extra glucose from the mother, they produce extra insulin to compensate for this, and ultimately this extra glucose is stored as fat

- Fetuses exposed to GDM appear to have a different growth trajectory than unexposed fetuses with excess weight in the trunk and shoulders

- This altered growth pattern and increased size places them at increased risk for birth injuries

Conway 2002 J Matern Fetal Neonatal Med
Kehl 1996 J Matern Fetal Neonatal Med
Catalano 2011 Semin Perinatol.
Das 2009 Arch Dis Child Fetal Neonatal Ed.

Timing of Delivery in GDM

Some authors have hypothesized that if women with GDM are delivered earlier, when their fetuses are smaller, this may reduce the risk of birth injuries

The Evidence

- 1 small single-centre RCT (n=200) conducted between 1987-1991 in LA in women with GDM or Type 2 diabetes who required insulin
  - At 38 weeks, women were randomized to induction of labour within 5 days vs. expectant management
  - Infants born following induction were significantly smaller (3446g vs. 3672g, $p<0.001$)
  - No cases of perinatal mortality, major congenital anomalies of hypoglycemia
  - Authors concluded that induction should be considered at 38 weeks

- Cochrane systematic review
  - Concluded that there was insufficient evidence to answer this question as there was only 1 small RCT

- Additional systematic review of observational studies also concluded that recommendations could not be made due to the low quality of evidence on this topic

Kjos 1993 Am J Obstet Gynecol
Boulvain 2001 Cochrane Database Sys Rev
Witkop 2009 Obstet Gynecol

This study aims to determine the optimal timing of delivery for women with GDM by quantifying the week-specific risks of maternal and perinatal morbidity and mortality in women who delivered following induction of labor or elective cesarean section compared to expectant management

Data was obtained from the Discharge Abstract Database on all singleton hospital deliveries in women with GDM and healthy controls in Canada (excluding Quebec) from 2004-2013

- As the focus of this study was identifying *optimal* timing of delivery, this cohort was restricted to pregnancies reaching at least 36 weeks of gestation

Primary outcomes included

- Severe maternal morbidity or mortality
  - Maternal death, obstetric embolism, obstetric shock, post-partum hemorrhage with hysterectomy or other procedures to control bleeding, sepsis, 3rd or 4th degree perineal laceration, uterine rupture, venous thromboembolism
- Severe perinatal morbidity or mortality
  - Stillbirth, neonatal death, birth asphyxia, fetal asphyxia, grade 3 or 4 intraventricular hemorrhage, neonatal convulsions, other disturbances of cerebral status of the newborn, respiratory distress syndrome, birth injuries, shoulder dystocia
- Neonatal morbidity due to increased size
  - Birth injuries or shoulder dystocia

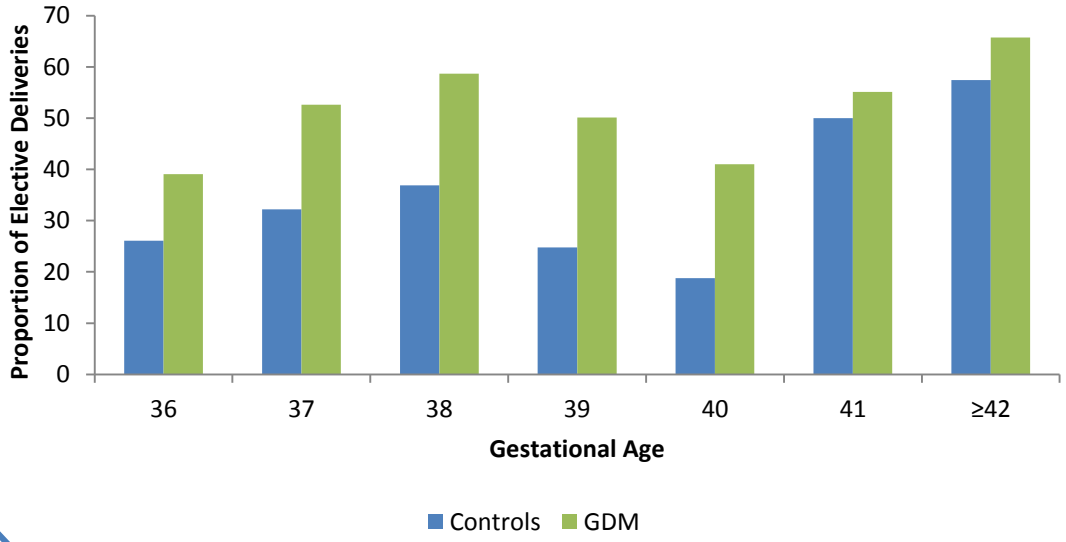
Traditional vs. Fetuses-At-Risk Approaches to Calculating Gestational-Age-Specific Rates

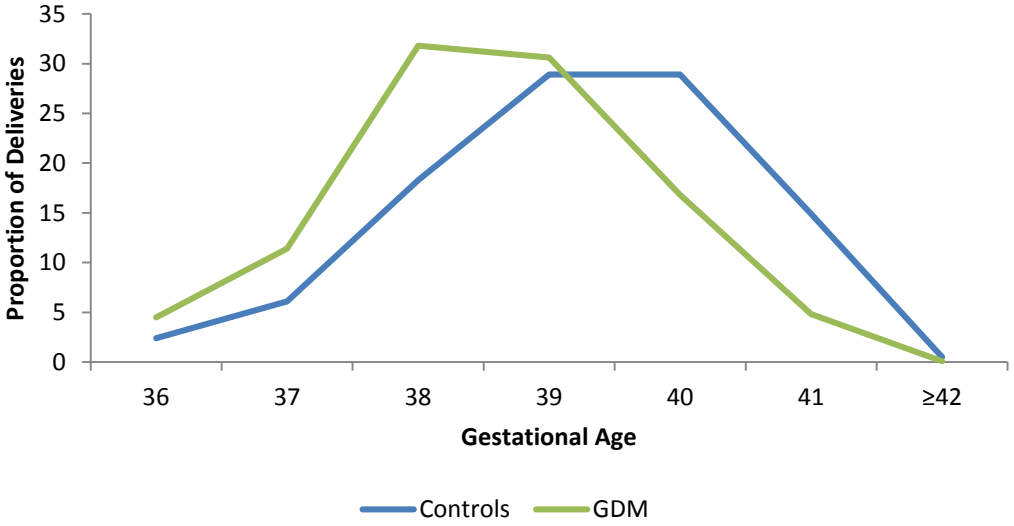
- Traditional Approach
  - Number of events at a specific gestational age are divided by the number of births at that gestational age
    - i.e. At 28 weeks of gestation, there were 39 stillbirths and 371 births, resulting in a stillbirth rate of 39/371=10.5%
  - Prognostic perspective – given a set of circumstances, which infants are more likely to do better than others
  - Gestational age is a determinant in predictive models

- Fetuses-At-Risk Approach
  - Number of events at a specific gestational age are divided by the number of fetuses in utero who were at risk of the event at that gestational age
    - i.e. At 28 weeks of gestation, there were 39 stillbirths and 317,634 ongoing pregnancies, resulting in a stillbirth rate of 39/317634=0.01%
  - Causal perspective – does a given set of circumstances cause an adverse outcome
  - Gestational age is a marker of survival time

Sample Characteristics

N=1,754,697 Healthy Controls
N=103,592 Women with GDM





Women with GDM were significantly more likely to have an elective delivery than controls ($p<0.001$)

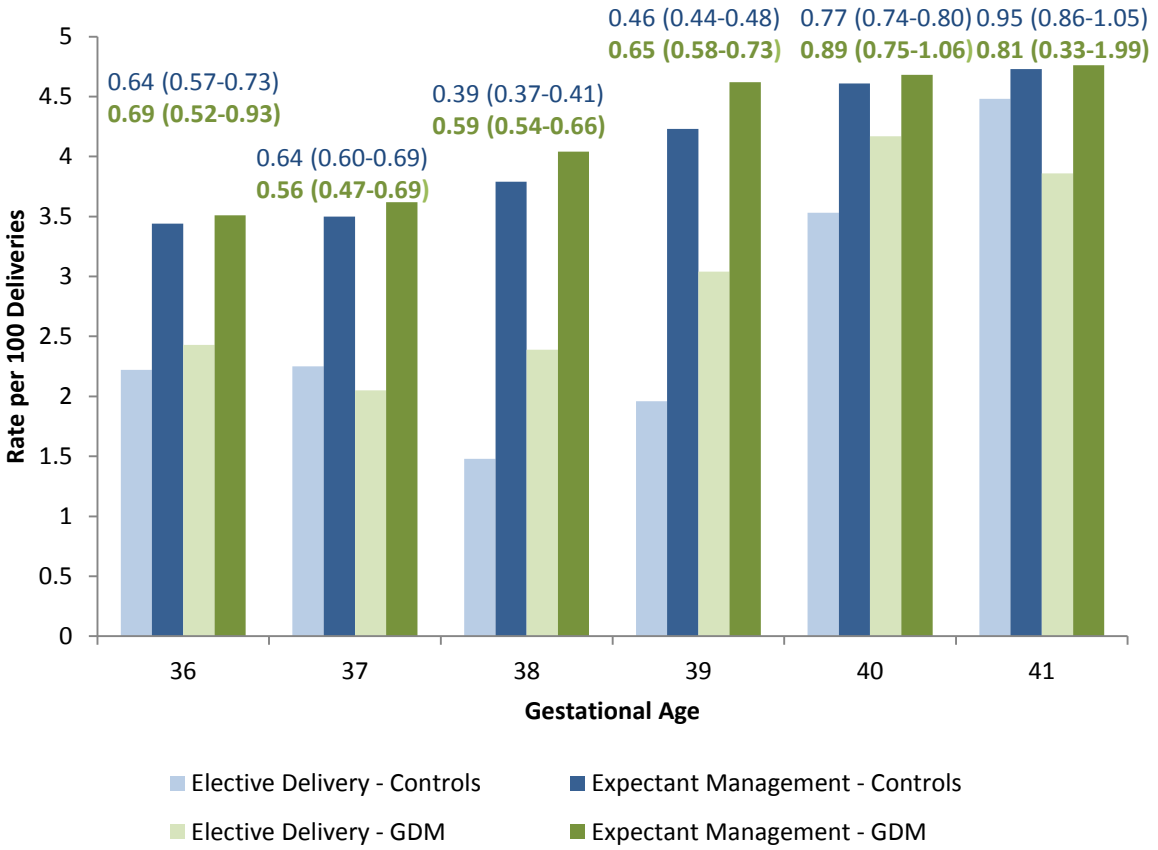
Severe Maternal Morbidity/Mortality

Overall, 3.41% (3.38-3.44) of healthy controls and 3.48% (3.37-3.59) of women with GDM experienced a severe maternal event (p=0.26)

3rd and 4th degree lacerations were the most common event

- Controls (3.07%) vs. GDM (2.98%), p=0.11

After excluding tears, 0.35% (0.34-0.36) of healthy controls and 0.51% (0.47-0.56) of women with GDM experienced a severe maternal event (p<0.001)



The rate of severe maternal morbidity/mortality was significantly lower with elective delivery from 36-40 weeks for controls and from 36-39 weeks for women with GDM.

When tears are excluded, expectant management is significantly favored in controls until 39 weeks of gestation. A1 41 weeks, elective delivery is preferred. While not reaching statistical significance, a similar pattern is observed in women with GDM.

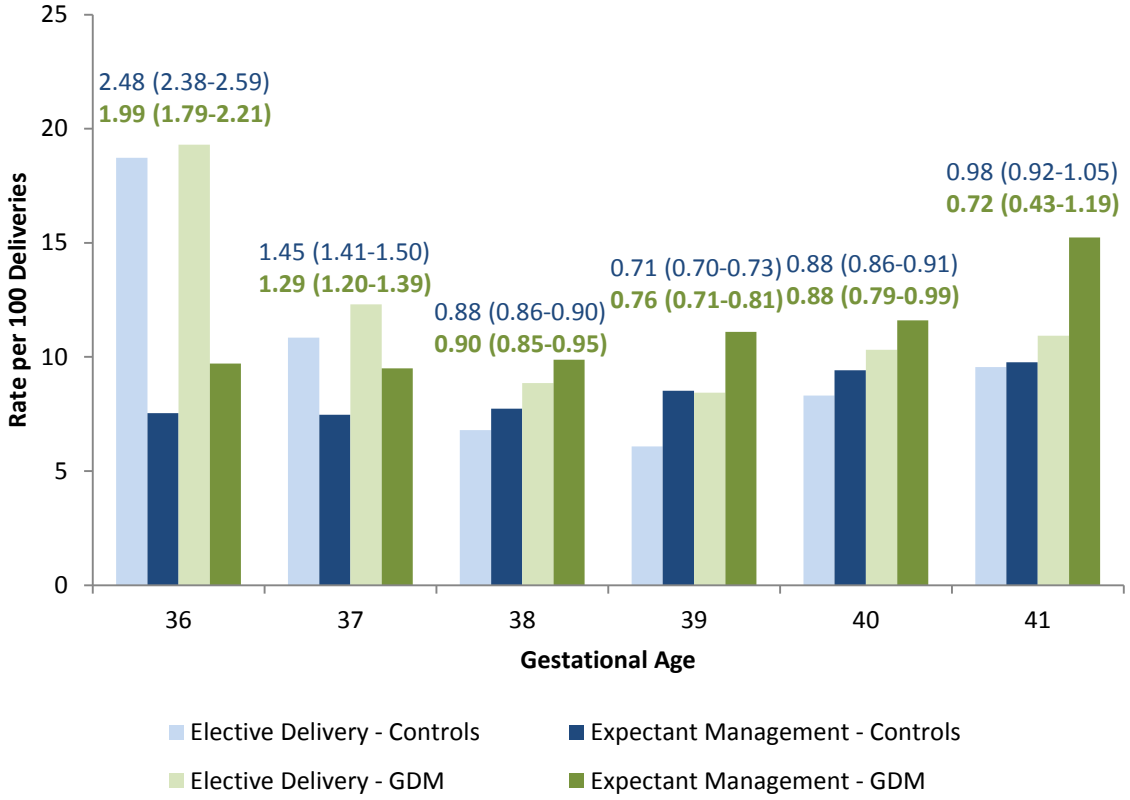
Severe Neonatal Morbidity/Mortality

Overall, 7.72% (7.68-7.76) of infants born to controls and 10.03% (9.85-10.22) of infants born to women with GDM experienced a severe neonatal event (p<0.001)

The most common causes of neonatal morbidity were:

- Shoulder Dystocia (Controls: 3.14%, GDM: 4.26%, p<0.001)
- Respiratory Distress Syndrome (Controls: 3.83%, GDM: 5.07%, p<0.001)

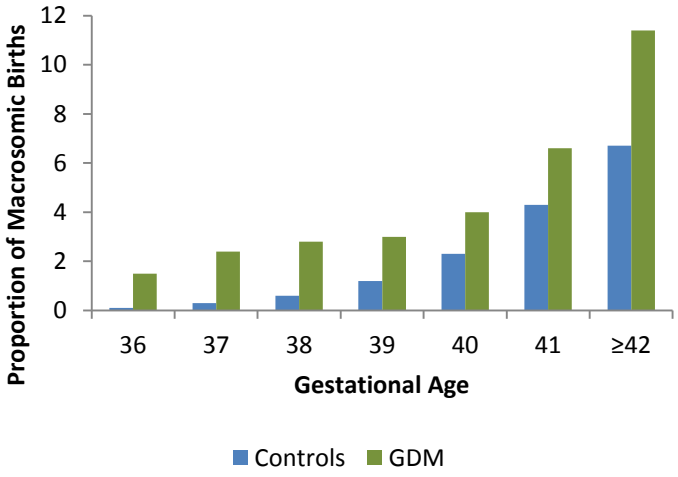
Perinatal mortality was rare in both groups (Controls 0.23%, GDM 0.35%, p<0.001)

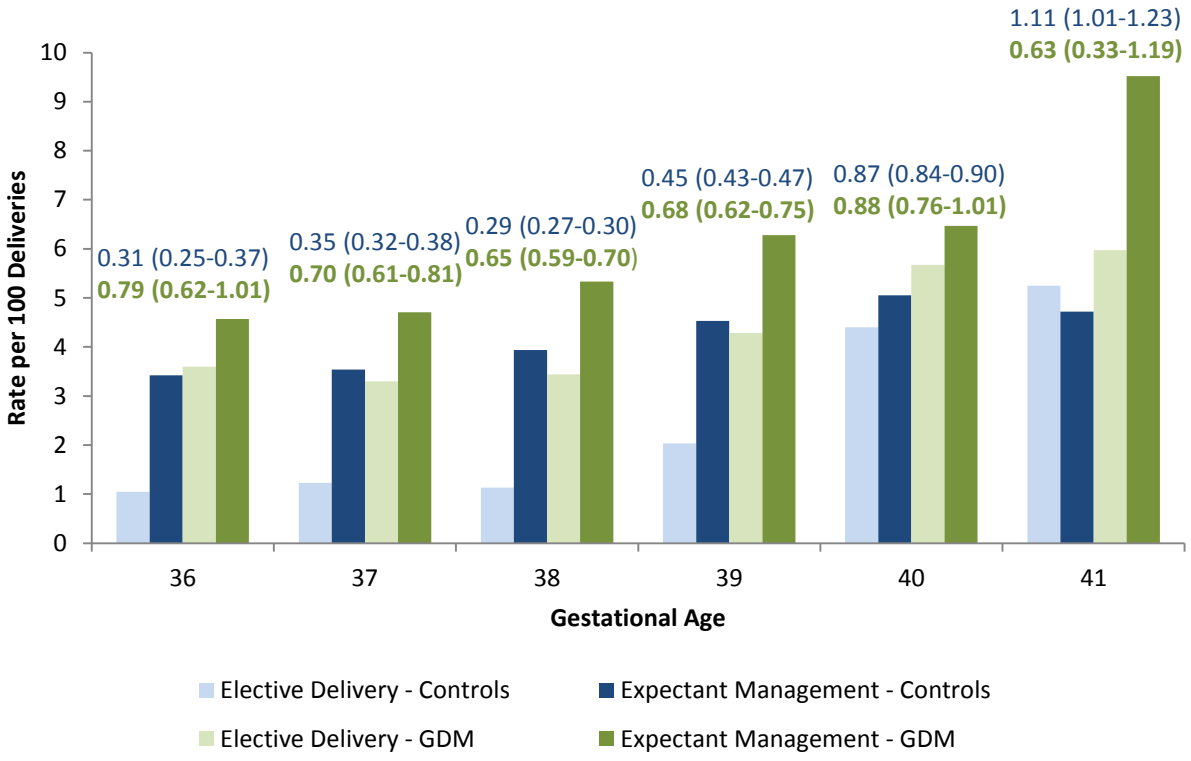


The rate of severe neonatal morbidity/mortality was significantly higher following elective delivery at 36 or 37 weeks for both controls and women with GDM. This pattern changed from 38-40 weeks for both groups whereby elective delivery was associated with significantly lower rates of severe neonatal morbidity/mortality.

Neonatal Morbidity Due to Increased Size

1.80% (1.79-1.83) of infants born to control women and 3.16% (3.05-3.26%) of infants born to women with GDM weighed ≥4500g at birth (p<0.001)





In women with GDM, elective delivery is significantly favored at 37-39 weeks (no significant differences observed at other time points), compared to control women where elective delivery is significantly favored prior to 41 weeks

Strengths and Limitations

- Strengths
  - Large population-based study with sufficient power to observe rare events
- Limitations
  - No clinical detail is available on how (or how well) GDM was managed
  - GDM may be under-ascertained

Conclusions

The clinical decision regarding elective delivery is complex and contingent on many factors related to both maternal and fetal wellbeing.

This study suggests that, similar to healthy women, elective delivery at 38 or 39 weeks of gestation optimizes maternal and neonatal outcomes among women with GDM

Questions?