ORIGINAL ARTICLE

Influence of medical nutrition therapy on borderline glucose intolerance in pregnant Taiwanese women

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Abstract

Objective: To investigate the influence of medical nutrition therapy (MNT) on borderline glucose intolerance (BGI) in pregnant Taiwanese women.

Methods: A total of 5194 singleton pregnant women were enrolled in this prospective, non-randomized study. The participants were subjected to the 50 g 1-h glucose challenge test (GCT) and 100 g 3-h oral glucose tolerance test (OGTT) to screening gestational diabetes mellitus (GDM). BGI was defined as a positive GCT and normal OGTT results. GDM was defined as a positive GCT and abnormal OGTT results. The women were categorized into the following groups: (1) GCT-negative, n = 3881; (2) BGI with MNT, n = 273; (3) BGI without MNT, n = 712; and (4) GDM, n = 328. Multiple logistic analyses were used to estimate the risks of pregnancy outcomes.

Results: The odds ratios (95% confidence interval) for total cesareans, third- or fourth-degree perineal lacerations, gestational hypertension or preeclampsia and macrosomia were 1.24 (1.04–1.49), 1.55 (1.06–1.28), 1.78 (1.21–2.61) and 2.50 (1.28–4.91) in the BGI without MNT group compared to the GCT-negative group. There was no difference between BGI with MNT and GCT-negative groups.

Conclusions: Women with BGI who did not receive MNT had increased risks of adverse pregnancy outcomes, whereas who received MNT had no different risk with GCT-negative women.

Keywords

Borderline glucose intolerance, excessive weight gain, gestational diabetes mellitus, medical nutrition therapy, pregnancy outcome

Introduction

The perinatal risks of gestational diabetes mellitus (GDM) are well documented [1]. Medical nutrition therapy (MNT) includes nutritional counseling, education, support and follow-up, which are required to assist the woman in making dietary and lifestyle changes [2–5]. Previous studies have indicated that MNT improves maternal and infant health outcomes for pregnant women with GDM [2,3,6–10].

Borderline glucose intolerance (BGI) is defined as a positive 50 g glucose challenge test (GCT) and ≤1 abnormal 100 g 3-h oral glucose tolerance test (OGTT) using a two-step approach for the screening and diagnosis of GDM. Previous studies have also shown that women with BGI during pregnancy also have significant adverse pregnancy outcomes [11–13]. Using a study population of 14,036 women, McLaughlin et al. [11] showed that women with positive GCT values and only one abnormal 100 g 3-h OGTT value are still at risk for adverse pregnancy outcomes. However, limited studies have compared pregnancy outcomes between women with BGI who did and did not receive MNT [14–17]. Deveer et al. [14] evaluated the effects of MNT for women who were diagnosed with BGI in a randomized controlled trial involving 100 pregnant women. Patients who were prescribed MNT by a dietitian had better pregnancy outcomes in terms of birth weights, numbers of large for gestational age (LGA) babies, macrosomia and total maternal weight gain during pregnancy. There have been no studies involving the full comparisons of the outcomes of healthy control groups (GCT-negative), BGI with MNT, BGI without MNT and GDM groups. These comparisons could comprehensively demonstrate the role of MNT in BGI. We hypothesized that women with BGI who receive MNT may “regress to normal outcomes” and have similar results as the healthy normal group (GCT-negative). In addition, women with BGI who do not receive MNT may “progress to worse outcomes” compared to the healthy normal group.

In this study, we evaluated the influence of MNT for BGI in pregnant women. The objective of this study was to

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compare excessive weight gain and pregnancy outcomes among the GCT-negative, BGI with MNT, BGI without MNT and GDM with MNT groups in a large, hospital-based sample.

**Materials and methods**

**Study design**

This is a prospective, non-randomized cohort study that enrolled all non-diabetic women with singleton pregnancies who delivered at one tertiary teaching hospital (1000 beds), the Ditmanson Medical Foundation Chia-Yi Christian Hospital (DMF-CYCH), in Taiwan between March 2011 and October 2013. The institutional review board of the DMF-CYCH approved this study (CYCH IRB No: 100006). All non-diabetic pregnant women in Taiwan have been asked to undergo GDM screening, and women with a positive GCT receive coverage from the National Health Insurance. Thus, all of the enrolled non-diabetic pregnant women in the study underwent a GCT. Exclusion criteria included women with overt diabetes and pre-existing hypertension or missing, incomplete or inadequate data. Due to the study objective of focusing on the influence of MNT, GDM patients who received intensive therapy (insulin injection or oral medication treatments) were considered to have inadequate data. In addition, women later than 32 weeks of gestation at study entry were also considered to have inadequate data (Figure 1).

A two-step approach according to the Carpenter and Coustan criteria was used [18]. Women underwent a 50-g 1-h GCT at 24–28 weeks of gestation. If the result of the GCT was ≥140 mg/dL, the women subsequently received a 100-g 3-h OGTT. Based on the results from the GCT and OGTT, BGI was defined as a positive GCT result and normal results on the 100-g OGTT. GDM was defined as a positive GCT result and abnormal results on the 100-g OGTT.

All pregnant with positive GCT results were recommended to receive MNT. Thus, based on whether the participant followed this recommendation, the enrolled pregnant women were categorized into the following four groups: (1) GCT-negative, GCT values < 140 mg/dL; (2) BGI with MNT; (3) BGI without MNT (usual prenatal care); and (4) GDM (subjects with abnormal results on a 100-g OGTT who were asked to receive MNT) (Figure 2).

**Medical nutrition therapy**

Nutritional counseling, dietary education, support and follow-up were provided by an integrated care team with collaboration of trained dietitians, nursing participants, case managers and physicians (including obstetrics and metabolism) [4,19]. MNT for BGI focuses on self-management and dietary education (food choices for appropriate weight gain, normoglycemia and the absence of ketones). The trained dietitian educated the women on controlling weight gain using the Institute of Medicine (IOM) 2009 guidelines to calculate the calories and carbohydrates in food and the self-monitoring of blood glucose (SMBG) (http://iom.edu/Reports/2009/Weight-Gain-During-Pregnancy-Reexamining-the-Guidelines.aspx). The diet consisted of 45–50% carbohydrate, 15–20% protein and 30–35% fat, which was divided into three meals and three snacks.

Figure 1. Flowchart describing study enrollees. GCT, glucose challenge test; OGTT, oral glucose tolerance test; BGI, borderline glucose intolerance; MNT, medical nutrition therapy; GDM, gestational diabetes mellitus.

Vegetables and high-fiber foods were encouraged. Repeated nutritional counseling and dietary education could be provided as requested by patients. Support and follow-up were performed by nursing participants, case managers and physicians using the outpatient management protocol as follows: one visit every 2 weeks to discuss MNT and ascertain compliance with diet education, to record the main clinical parameters (weight, blood pressure and urine test results, etc.), and to discuss the case among the integrated care team.

**Outcome variables**

Weight gain during pregnancy was measured according to the IOM 2009 guidelines; however, because the body mass index (BMI) in Asian women is lower than that in Western women, BMI in this study was classified as follows: <18.5 (underweight), 18.5–24 (normal), 24–27 (overweight), ≥27 kg/m² (obese), according to the Bureau of Health Promotion, Department of Health, Taiwan (http://health99.hpa.gov.tw/OnlinkHealth/Onlink_BMI.aspx). Excessive weight gain was defined as weight gain during pregnancy that exceeded the modified guidelines. Pre-pregnancy weight was ascertained from the patient’s pre-pregnancy records (Supplemental Table S1).

The pregnancy outcomes included maternal complications, such as cesarean section, prolonged labor, shoulder dystocia,
third- or fourth-degree perineal laceration, postpartum hemorrhage and gestational hypertension or preeclampsia, in addition to neonatal complications, such as preterm delivery (<37 weeks), admission to the neonatal intensive care unit (NICU), low birth weight (<2500 g), macrosomia (>4000 g) and Apgar scores of <7 at 1 and 5 min. Gestational hypertension was defined as blood pressure ≥140 mmHg systolic or ≥90 mmHg diastolic after 20 weeks of gestation in women with previously normal blood pressure whose blood pressure levels returned to normal in the postpartum period. Preeclampsia was characterized by gestational hypertension and proteinuria (≥0.3 g/day or ≥1+ on a urine dipstick) with or without pathologic edema.

Statistics analysis

The differences between the four groups were analyzed using the analysis of variance (ANOVA) test for continuous variables according to the central limit theorem. If the means significantly differed, a post hoc multiple comparison test using the Tukey’s studentized range (HSD) was performed. The chi-squared test or Fisher’s exact test was used for the categorical variables. Multiple logistic analyses were used to determine the risks of excessive weight gain among the four groups after adjusting for nulliparous status, maternal age and prepregnancy BMI. The multiple logistic analyses were used to determine the risks of adverse pregnancy outcomes among the four groups after adjusting for nulliparous status, maternal age, pre-pregnancy BMI and excessive weight gain. Pre-pregnancy BMI was calculated as pre-pregnancy weight divided by height squared (kg/m²). A two-sided p value < 0.05 was considered to be statistically significant. All of the data were merged, and the analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC).

Results

A total of 6302 women with singleton pregnancies who underwent the 50-g GCT at 24–28 weeks of gestation and who delivered at the DMF-CYCH were enrolled during the study period. Among them, 502 women with missing prepregnancy weight and weight at study entry data and 50 women with overt diabetes and pre-existing hypertension were excluded. An additional 123 women were excluded from the analyses due to incomplete OGTT data, and 163 were excluded due to inadequate data, including 17 who received insulin or oral diabetic treatments and 146 whose gestational age at study entry was over 32 weeks. Thus, all women with GDM were asked to receive MNT and no GDM patients who were included in the study received insulin or oral medications. Finally, a total of 5194 women were included in the final analyses. Of these women, 3881 (74.7%) screened negative, 273 (5.3%) were had BGI and received MNT, 712 (13.7%) had BGI and did not receive MNT and 328 (6.3%) had GDM and received MNT (Figure 1).

Table 1 describes the characteristics and 50-g GCT levels of the study participants. With the exception of nulliparous status, the four groups significantly differed. After the post hoc multiple comparisons, there were no significant differences between the BGI with MNT and BGI without MNT groups with the exception of the gestational week at study entry (Supplemental Table S2).
Table 1. Characteristics and glucose results of the study population.

| Variable                           | GCT-negative (n = 3881) | BGI with MNT (n = 273) | BGI without MNT (n = 712) | GDM (n = 328) | p   |
|------------------------------------|-------------------------|------------------------|---------------------------|--------------|-----|
| Nulliparous status                 |                         |                        |                           |              |     |
| Yes                                | 1942 (50.0)             | 139 (50.9)             | 358 (50.3)                | 144 (43.9)   | 0.18|
| No                                 | 1939 (50.0)             | 134 (49.1)             | 354 (49.7)                | 184 (56.1)   |     |
| Maternal age (years)               | 29.7 ± 4.6              | 30.7 ± 4.5             | 31.2 ± 4.4                | 32.6 ± 4.7   |     |
| Pre-pregnancy BMI (kg/m²)          | 21.5 ± 3.4              | 21.8 ± 3.6             | 22.4 ± 4.0                | 23.4 ± 4.2   | <0.001|
| Gestational week at study entry    | 29.5 ± 1.4              | 27.5 ± 1.7             | 28.7 ± 1.8                | 28.8 ± 1.8   | <0.001|
| Gestational week at delivery       | 38.4 ± 1.4              | 38.2 ± 1.4             | 38.3 ± 1.4                | 38.0 ± 1.5   | <0.001|
| Weight gain during pregnancy (kg)  | 13.4 ± 4.7              | 12.5 ± 4.8             | 12.9 ± 4.7                | 11.8 ± 4.9   | <0.001|
| 50-g GCT levels (mg/dL)            | 111.5 ± 16.5            | 156.9 ± 16.7           | 158.5 ± 15.9              | 173.8 ± 25.2 | <0.001|
| 100-g OGTT levels (mg/dL)          |                         |                        |                           |              |     |
| Fasting                            | –                       | 82.3 ± 6.0             | 83.3 ± 6.6                | 89.8 ± 10.4  | <0.001|
| 1 h                                | –                       | 150.6 ± 23.5           | 150.2 ± 23.9              | 193.3 ± 25.2 | <0.001|
| 2 h                                | –                       | 130.6 ± 20.0           | 131.1 ± 20.8              | 175.6 ± 23.0 | <0.001|
| 3 h                                | –                       | 106.4 ± 19.6           | 108.3 ± 22.0              | 135.6 ± 29.8 | <0.001|

GCT, glucose challenge test; BGI, borderline glucose intolerance; MNT, medical nutrition therapy; GDM, gestational diabetes mellitus; BMI, body mass index; OGTT, oral glucose tolerance test. Categorical data are presented as n (%) and assessed using the chi-square test; continuous data are presented as means ± standard deviation and assessed using the ANOVA and post hoc multiple comparisons tests using the Tukey's studentized range (HSD) test (Supplemental Table S2).

Table 2. Associations of excessive weight gain and pregnancy outcomes among the GCT-negative, BGI with MNT, BGI without MNT and GDM groups.

| Outcome variable                          | Number | GCT-negative (n = 3881) | BGI with MNT (n = 273) | BGI without MNT (n = 712) | GDM (n = 328) | p   |
|-------------------------------------------|--------|-------------------------|------------------------|---------------------------|--------------|-----|
| Excessive weight gain*                    | 1702/5194 | 1291/3881 (33.3)        | 76/273 (26.3)          | 229/712 (32.2)            | 106/328 (32.3) | 0.31|
| Delivery mode                             |        |                        |                        |                           |              |     |
| Total cesareans                           | 1461/5194 | 1020/3881 (26.3)        | 80/273 (29.3)          | 240/712 (33.7)            | 121/328 (36.9) | <0.001|
| Cesarean due to prolonged labor, macrosomia or disproportion| 364/5194 | 260/3881 (6.7)         | 18/273 (6.6)          | 61/712 (8.6)             | 25/328 (7.6)  | 0.32|
| Maternal outcomes                         |        |                        |                        |                           |              |     |
| Prolonged labor                           | 891/5194 | 685/3881 (17.7)         | 44/273 (16.1)          | 122/712 (17.1)           | 40/328 (12.2) | 0.09|
| Shoulder dystocia¶                         | 51/3733 | 38 (1.3)                | 0 (0.0)                | 8 (1.7)                   | 5 (2.4)       | 0.15|
| Third- or fourth-degree perineal laceration| 206/3733 | 151 (5.3)               | 5 (2.6)                | 38 (8.1)                  | 12 (5.8)      | 0.03|
| Postpartum hemorrhage                     | 38/5194 | 26 (0.7)                | 2 (0.7)                | 7 (1.0)                   | 3 (0.9)       | 0.67|
| Gestational hypertension or preeclampsia   | 183/5194 | 110 (2.8)               | 7 (2.6)                | 42 (5.9)                  | 24 (7.3)      | <0.001|
| Neonatal outcomes                         |        |                        |                        |                           |              |     |
| Preterm delivery (<37 weeks)              | 319/5194 | 218 (5.6)               | 17 (6.2)               | 56 (7.9)                  | 28 (8.5)      | 0.03|
| Admission to NICU*                         | 418/5185 | 286 (7.4)               | 23 (8.5)               | 72 (10.1)                 | 37 (11.3)     | 0.01|
| Low birth weight (<2500 g)                | 307/5194 | 217 (5.6)               | 20 (7.3)               | 47 (6.6)                  | 23 (7.0)      | 0.39|
| Macrosomia (>4000 g)                      | 53/5194 | 29 (0.8)                | 0 (0.0)                | 14 (2.0)                  | 10 (3.1)      | <0.001¶|
| Apgar score <7 at 1 min                   | 83/5194 | 56 (1.4)                | 5 (1.8)                | 15 (2.1)                  | 7 (2.1)       | 0.48|
| Apgar score <7 at 5 min                   | 30/5194 | 20 (0.5)                | 1 (0.4)                | 8 (1.1)                   | 1 (0.3)       | 0.23|

GCT, glucose challenge test; BGI, borderline glucose intolerance; MNT, medical nutrition therapy; GDM, gestational diabetes mellitus; NICU, neonatal intensive care unit. Data are presented as n (%).

*Excessive weight gain was modified according to the Institute of Medicine 2009 guidelines.

†Excluding elective cesarean section and scheduled cesarean section due to previous cesarean section, placenta previa and malposition and malpresentation of the fetus.

‡Only included vaginal delivery.

*Excluded neonatal death.

¶Fisher’s exact test was performed.

Table 2 demonstrates associations of excessive weight gain and pregnancy outcomes among the GCT-negative, BGI with MNT, BGI without MNT and GDM groups. The prevalence of total cesareans, third- or fourth-degree perineal lacerations, gestational hypertension or preeclampsia, preterm deliveries, NICU admissions and macrosomia significantly differed among the four groups (p < 0.05). There was no macrosomia observed in the BGI with MNT group. The rate of third- or fourth-degree perineal lacerations and gestational hypertension or preeclampsia were lower in the BGI with MNT group compared with the BGI without MNT group and were even lower in comparison with the GCT-negative group.

Table 3 shows the adjusted odds ratios for excessive weight gain and adverse pregnancy outcomes using multiple logistic regression analyses. Compared to the GCT-negative group, the risk of excessive weight gain did not differ among the three GCT-positive groups. In the BGI without MNT group, the odds ratios (95% confidence interval) for total cesareans, third- or fourth-degree perineal lacerations, gestational hypertension or preeclampsia and macrosomia were 1.24
Table 3. Estimated risk of the excessive weight gain and adverse pregnancy outcomes in the BGI with MNT, BGI without MNT and GDM groups compared with the GCT-negative group.

| Outcome variables                        | GCT-negative (n = 3881) | BGI with MNT (n = 273) | BGI without MNT (n = 712) | GDM (n = 328) |
|------------------------------------------|-------------------------|------------------------|---------------------------|--------------|
| Excessive weight gain*                   | 1                       | 0.79 (0.59–1.07)       | 0.89 (0.74–1.07)          | 0.82 (0.63–1.07) |
| Delivery mode                            |                         |                        |                           |              |
| Total cesareans                          | 1                       | 1.10 (0.82–1.47)       | 1.24 (1.04–1.49)          | 1.23 (0.96–1.58) |
| Cesarean due to prolonged labor, macrosomia or disproportion† | 1                       | 0.86 (0.51–1.47)       | 1.16 (0.85–1.58)          | 1.03 (0.65–1.65) |
| Maternal outcomes                        |                         |                        |                           |              |
| Prolonged labor                          | 1                       | 0.98 (0.69–1.39)       | 1.02 (0.82–1.26)          | 0.70 (0.49–0.99) |
| Shoulder dystocia;§                      | 1                       | –                      | 1.31 (0.60–2.90)          | 1.71 (0.64–4.58) |
| Third- or fourth-degree perineal laceration‡ | 1                       | 0.47 (0.19–1.17)       | 1.55 (1.06–2.28)          | 1.15 (0.61–2.16) |
| Postpartum hemorrhage                    | 1                       | 1.37 (0.30–6.25)       | 1.51 (0.64–3.58)          | 1.35 (0.39–4.68) |
| Gestational hypertension or preeclampsia | 1                       | 0.84 (0.38–1.89)       | 1.78 (1.21–2.61)          | 1.96 (1.19–3.21) |
| Neonatal outcomes                        |                         |                        |                           |              |
| Preterm delivery (<37 weeks)             | 1                       | 0.89 (0.52–1.53)       | 1.23 (0.90–1.69)          | 1.19 (0.77–1.84) |
| Admission to NICU*                       | 1                       | 1.01 (0.63–1.62)       | 1.24 (0.94–1.65)          | 1.28 (0.87–1.87) |
| Low birth weight (<2500 g)               | 1                       | 1.07 (0.64–1.77)       | 1.08 (0.77–1.51)          | 1.11 (0.69–1.77) |
| Macrosomia (>4000 g)§                    | 1                       | –                      | 2.50 (1.28–4.91)          | 3.60 (1.64–7.90) |
| Apgar score <7 at 1 min                  | 1                       | 0.97 (0.36–2.57)       | 1.17 (0.64–2.13)          | 0.99 (0.43–2.30) |
| Apgar score <7 at 5 min                  | 1                       | 0.49 (0.06–3.91)       | 1.66 (0.70–3.96)          | 0.36 (0.05–2.82) |

GCT, glucose challenge test; BGI, borderline glucose intolerance; MNT, medical nutrition therapy; GDM, gestational diabetes mellitus; NICU, neonatal intensive care unit. Data are presented as odds ratios (95% confidence interval) and adjusted for nulliparous status, maternal age, pre-pregnancy BMI, gestational week at study entry and excessive weight gain.

*Excessive weight gain was modified according to the Institute of Medicine 2009 guidelines.
†Excluding elective cesarean section and scheduled cesarean section because of previous cesarean section, placenta previa and malposition and malpresentation of the fetus.
‡Only included vaginal delivery.
§Excluded neonatal death.
¶Excluded the BGI with MNT group because no events occurred.

Discussion

In this study, we used a large prospective, non-randomized population comparing excessive weight gain and pregnancy outcomes in women who were GCT-negative, those with BGI who did or did not receive MNT, and those with GDM who received MNT. Our findings indicate that the BGI without MNT group had significantly higher risks of total cesareans, third- or fourth-degree perineal lacerations, gestational hypertension or preeclampsia and macromia compared to the GCT-negative group. In contrast, there was no difference between the BGI with MNT- and GCT-negative groups.

One large-sample study demonstrated increased risks of maternal outcomes, including cesarean deliveries and preeclampsia, in women with one elevated 3-h glucose tolerance test value [11]. Bevier et al. reported that women who were treated for BGI exhibited improved outcomes, including reduced frequencies of cesarean sections [16]. Our results indicate that the risk of caesarean was significantly higher in the BGI without MNT group compared with that of the GCT-negative group. The BGI with MNT group displayed a 53% decreased risk of perineal lacerations (although not significant), and the BGI without MNT group showed a 55% significantly increased risk. Surprisingly, the BGI without MNT group had an even higher risk than the GDM with MNT group. Conversely, women with BGI who did not receive MNT showed the highest risks. There were 78 and 96% increased risks of gestational hypertension and preeclampsia in the BGI without MNT and GDM with MNT groups compared with the GCT-negative group, respectively. We have provided supporting evidence to indicate that BGI is harmful to pregnant women and that its harmful effects may be reversed by MNT.

Previous studies have shown that women with abnormal GCT values (but normal 100-g 3-h OGTT values) display decreased prevalence of adverse neonatal outcomes, including preterm labor, LGA babies, macrosomia and NICU admissions [11–13]. Some previous studies have shown that the frequency of large-sized infants is significantly lower following BGI treatment [14,15,17]. In our analysis, the GDM group displayed a 3.6-fold increased risk of macromia compared with that of the GCT-negative group. The BGI without MNT group had a similar risk of macromia. The BGI with MNT group had no cases of macromia. Macrosomia seems to be a consistent and sensitive risk factor for adverse delivery outcomes involving glucose metabolism. The effects and feasibility of the control of GDM and BGI on macrosomia should be further investigated [20].

The strength of this study was its large sample size, the obstetrician-led MNT program provided by an integrated care team, and the comparison of four groups (including GDM patients) based on both glucose test results and MNT to avoid sample selection bias. To facilitate a fair comparison, we also excluded patients who received insulin and/or oral anti-diabetes drugs, women who received MNT after 32 weeks of...
gestation, or those who did not return to the obstetrics clinic for their usual prenatal care after undergoing the screening tests.

There were several limitations in this study. First, given the intention to receive MNT nature of the study design, there was a potential for bias in the selection of individuals who received MNT. To address this concern, we have performed post hoc multiple comparisons that showed no significant differences between the BGI with MNT and BGI without MNT groups. Furthermore, we used multiple logistic regression analysis to estimate the impacts of MNT adjusted for the known risk factors. However, there may have been other characteristics that biased the team to provide treatment to the MNT groups, such as higher level of education, employment and demonstrated reliability in keeping appointments; these data are not available. Second, the study focused on Taiwanese women and may not be generalizable to other ethnic populations. Third, multi-center, multi-ethnic, randomized trials are still needed.

Conclusion

Our findings indicate that MNT influences adverse pregnancy outcomes among women with BGI. Women with BGI who did not receive MNT had increased risks of adverse pregnancy outcomes, whereas who received MNT reduced the risk. We suggested that an obstetrician-led MNT program provided by an integrated care team is necessary for women who have been diagnosed with BGI in prenatal care.

Declaration of interest

No specific funding was obtained for this study.

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Supplementary material available online.
Supplemental Tables S1 and S2.