Received: 1 August 2023 | Revised: 16 October 2023 | Accepted: 24 October 2023

DOI: 10.1111/mcn.13589

ORIGINAL ARTICLE

Maternal & Child Nutrition WILEY

# Dietary supplements, guideline alignment and biochemical nutrient status in pregnancy: Findings from the Queensland Family Cohort pilot study

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**Funding information**
Griffith University; Queensland University of Technology; University of the Sunshine Coast; University of Queensland; Mater Foundation

## Abstract

In high-income nations, multiple micronutrient (MMN) supplementation during pregnancy is a common practice. We aimed to describe maternal characteristics associated with supplement use and daily dose of supplemental nutrients consumed in pregnancy, and whether guideline alignment and nutrient status are related to supplement use. The Queensland Family Cohort is a prospective, Australian observational longitudinal study. Maternal characteristics, nutrient intake from food and supplements, and biochemical nutrient status were assessed in the second trimester ($n$ = 127). Supplement use was reported by 89% of participants, of whom 91% reported taking an MMN supplement. Participants who received private obstetric care, had private health insurance and had greater alignment to meat/vegetarian alternatives recommendations were more likely to report MMN supplement use. Private obstetric care and general practitioner shared care were associated with higher daily dose of supplemental nutrients consumed compared with midwifery group practice. There was high reliance on supplements to meet nutrient reference values for folate, iodine and iron, but only plasma folate concentrations were higher in MMN supplement versus nonsupplement users. Exceeding the upper level of intake for folic acid and iron was more likely among combined MMN and individual supplement/s users, and associated with higher plasma concentrations of the respective nutrients. Given the low alignment with food group recommendations and potential risks associated with high MMN supplement use, whole food diets should be emphasized. This study confirms the need to define effective strategies for optimizing nutrient intake in pregnancy, especially among those most vulnerable where MMN supplement use may be appropriate.

KEYWORDS
birth cohort, dietary intake, dietary guidelines, supplement guidelines, supplementation

## 1 | INTRODUCTION

Maternal dietary patterns and nutrient status have long been recognized to impact both maternal and child health outcomes (Marangoni et al., 2016). Nutritionally high-quality diets that are rich in fruits, vegetables, legumes, nuts and fish are associated with reduced risk of inadequate or excessive gestational weight gain, gestational diabetes mellitus, pre-eclampsia, anaemia, preterm birth or miscarriage and long-term maternal overweight, obesity, type 2 diabetes mellitus and cardiovascular disease (Grieger et al., 2014; Schoenaker et al., 2015, 2016; Tobias et al., 2012). Improved infant outcomes include achieving optimal birth weight, better immune function and reduced risk of noncommunicable diseases in childhood and adulthood (Gernand et al., 2016).

The Australian Guide to Healthy Eating provides evidence-based recommendations on the types and amounts of food that should be eaten, including the increased food requirements to meet nutritional needs in pregnancy (National Health and Medical Research Council, 2013). It is recommended that a variety of nutritious foods are consumed, including whole fruits and vegetables of different types and colours, dairy or calcium-enriched alternatives and increased daily serves of wholegrains and iron-rich foods, such as lean red meat or tofu. Studies indicate that dietary patterns commonly fall short of these guidelines. For example, two recent Australian studies reported that only ~40%, ~25% and ~12% of pregnant people consumed the recommended serves of fruit, vegetable/legume and dairy/alternatives, respectively (Slater et al., 2020; Wilkinson et al., 2022). The higher recommendation for grains and meat/vegetarian alternatives was met by less than 1% and less than 20% of pregnant people, respectively (Slater et al., 2020; Wilkinson et al., 2022). This is consistent with a systematic review of dietary intakes during pregnancy in high-income countries that found energy and fibre intakes were consistently below national recommendations (Blumfield et al., 2012).

**Key messages**

- Multiple micronutrient (MMN) supplementation during pregnancy is a common practice in high-income countries.
- Participants who received private obstetric care, had private health insurance and had greater alignment to meat/vegetarian alternatives recommendations were more likely to report MMN supplement use.
- There was high reliance on supplements to meet intake guidelines for folate, iodine and iron, which also raised concern for excess nutrient intake.
- This study confirms the need to define effective strategies for optimizing nutrient intake in pregnancy, including the promotion of whole food diets and appropriate use of MMN supplements.

In Australia, supplementation with vitamins and minerals is common practice. Among those who self-reported taking at least one dietary supplement during preconception (~60%) and/or throughout pregnancy (~90%), the most commonly reported product was a multiple micronutrient (MMN) supplement (Livock et al., 2017; McKenna et al., 2017). This is despite Australian recommendations for supplement intake during pregnancy consisting only of folic acid (1 month preconception to 3 months of pregnancy) and iodine (throughout pregnancy) (Australian Government Department of Health and Aged Care, 2020). Other individual supplements (e.g., vitamin B12, vitamin D, iron, calcium and omega-3 fatty acids) are recommended for people with a diagnosed deficiency, pre-eclampsia risk or for those who avoid certain food groups, such as meat/vegetarian alternatives (Australian Government Department of Health and Aged Care, 2020). Although MMN supplementation in pregnancy in low and middle-income countries improves gestational weight gain, birth weight and may reduce preterm births (Keats et al., 2019; Liu et al., 2022), there is no evidence for childhood health benefits (Devakumar et al., 2016) and the potential benefits and/or harms for people in high-income countries remains inconclusive (Petry et al., 2020; Raghavan et al., 2018; Wolf et al., 2017).

This aims of this study were as follows: (1) to describe the types of supplements taken in pregnancy by maternal characteristics; (2) identify whether supplement use and/or type affect alignment with nutrient target recommendations and plasma concentrations of folate, zinc, calcium, iodine and iron, and urine iodine levels; and (3) assess whether mean daily dose of supplemental nutrients could be predicted by certain maternal characteristics. These data may allow for targeted advice to help optimize dietary patterns throughout pregnancy.

## 2 | MATERIALS AND METHODS

### 2.1 | Study participants

The study was approved by the Mater Misericordiae Ltd Human Research Ethics Committee (HREC/MML/61205) and ratified by The University of Queensland Human Research Ethics Committee (2020001491) and University of the Sunshine Coast Office of Research (A221762). The current study constituted part of a large pilot study, Queensland Family Cohort, which included a series of other assessments and questionnaires, and the intent to follow up families for three decades (Borg et al., 2021). People who were 12–24 weeks pregnant and were booked to give birth at the Mater Mothers' Hospitals in 2019 were eligible to participate (Figure 1). Pregnant people could tick a box on their hospital booking sheet to confirm their interest in research. If interested, they were contacted via SMS by a research midwife and sent the study information and consent sheet via email. If people did not respond to the email, a research midwife followed up by phone call. The study was also advertised inside Mater antenatal clinics using display screens and posters. Informed consent was obtained. Maternal characteristics were collected at 22 weeks via questionnaire and included race, date of birth and estimated due date (to calculate participant age), prepregnancy height and weight (to calculate body mass index [BMI]), parity, conception details (planned/unplanned and spontaneous/assisted), model of antenatal care (general practitioner [GP] shared care; private obstetrician; midwifery hospital care; midwifery group practice; or other specialist care, e.g., midwifery group practice for young mothers, indigenous or refugee, combined midwifery/obstetric care; diabetes management), postcode of residence (to calculate tertiles of Socioeconomic Indexes for Areas (SEIFA 2016) index of relative socioeconomic advantage and disadvantage), weekly household income after tax, private health insurance, highest level of education and diagnosed medical conditions. Diagnosed anaemia at 28 weeks' gestation was also identified via a study survey on pregnancy complications. Data on birth outcomes were also collected including mode of birth onset, delivery type, sex, birth weight, gestational age at delivery, small for gestational age for sex (birth weight <10th centile as per Fenton growth chart), preterm birth (<37 weeks' gestation) and admission to neonatal intensive care unit or special care nursery.

### 2.2 | Nutrient intake from diet and/or supplements

Dietary intakes in this cohort, including food group and nutrient alignment with national recommendations, has been published previously but this did not include dietary supplements taken or its contribution to nutrient adequacy (Wilkinson et al., 2022). Briefly, information about dietary intake over the previous 3–6 months was self-reported at 24 weeks' gestation using the 120-item Australian Eating Survey (AES) semiquantitative Food Frequency Questionnaire (Collins et al., 2015). The frequency options within the AES ranged from 'Never' up to '≥4 times/day', but varied depending on the food, with some drinks items up to '≥7 glasses/day'. Standard portion sizes were derived for AES items using data from the National Nutrition Survey (Australian Bureau of Statistics, 1998). Nutrient intakes from food alone were computed using data in the AUSNUT 2011–13 database (Food Standards Australia New Zealand, 2014). Specifically, daily intakes of folate (as dietary folate equivalents [DFE]), zinc, calcium, iodine and iron were computed. A measure of diet quality, the Australian Recommended Food Score (ARFS), was calculated as an AES subscale with a maximum score of 73 (Ashton et al., 2017; Collins et al., 2015). A subset of 70 AES food items are used to calculate the ARFS. It comprises eight subscales from core food groups of vegetables, fruit, grains, meats, nonmeat proteins and dairy, with a total score ranging from 0 to 73. For most items, AES frequency response options are collapsed into two categories 'once per week or more' or 'less than once per week or never' (Collins et al., 2015).

Information on supplements were collected by a Research Midwife using a Medication and Lifestyle questionnaire at 28 weeks' gestation. Supplement intake was current at time of survey completion and, therefore, some participants may have been taking the reported supplement/s since preconception, whereas others may have only recently commenced. The concentrations of folic acid, zinc, calcium, iodine and iron in reported supplement brands were determined and, where a participant could not recall the brand name, a conservative estimate of nutrient content was applied based on all brands reported within this cohort. Participants were given several options for frequency of supplement intake. The responses 'varies/as required', '1 to 2 times/week', '3 or more times/week' and 'every day and/or night' were assigned an intake of 0, 2, 3 and 7 days per week, respectively. Weekly intake of each nutrient from all supplements was calculated and divided by 7, to obtain mean daily dose of supplemental nutrients.

Total daily intakes of folate (DFE), zinc, calcium, iodine and iron from food and supplements combined were compared with estimated average requirements (EAR) and excess nutrient intakes were compared with the upper level of intake (UL) using the Nutrient

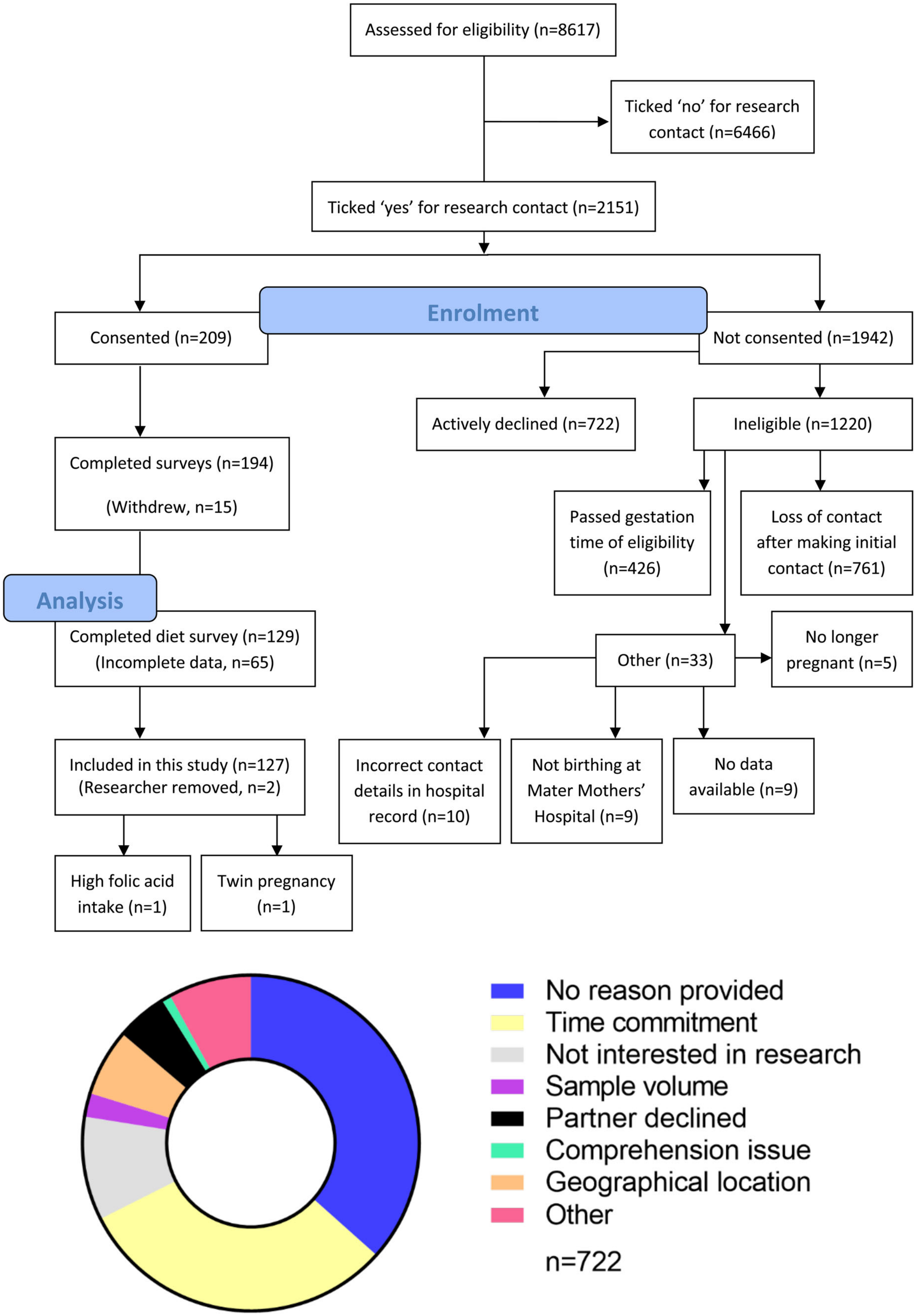


**FIGURE 1** STROBE flowchart for participant inclusion in the Queensland Family Cohort study, which included a series of other assessments unrelated to the current study and longitudinal follow up.

Reference Values for Australia and New Zealand (National Health and Medical Research Council, 2006). Total daily intake of folate (DFE) was calculated by: DFE in food + (mean daily dose of supplemental folic acid × 1.67). DFE considers the higher bioavailability of folic acid used to fortify foods and in supplements (85%) compared with natural folates in food (50%–60%) (National Health and Medical Research Council, 2006).

### 2.3 | Biochemical nutrient status

A blood sample was collected at 28 weeks and plasma concentrations of calcium, zinc, iron, folate and iodine were measured. Urine iodine concentration was also measured at 28 weeks. Plasma calcium, zinc, iron and iodine concentrations were measured using inductively coupled plasma mass spectrometry (ICP-MS), as previously described (McKeating et al., 2020). Plasma folate concentration was measured using the Cobas e411 immunoanalyzer and relevant assay reagents (Elecsys Folate III assay, calibrator set and diluent universal from Roche Diagnostics). Plasma samples were briefly centrifuged and a minimum of 200 µL transferred to a clean tube for measurement. Samples above the assay range (1.36–45.4 nM) were diluted 1:1 with diluent universal and a further 1:1 serial dilution where necessary. Duplicate analysis was done on 20 samples to determine an overall coefficient of variation of 4.7%. Urinary iodine was measured using an Agilent 7900 ICP-MS in samples diluted 10-fold in the following matrix: 2% (v/v) $NH_4OH$ (28%, 99.99% purity), 4% (v/v) isopropanol (AR grade) and 0.1% w/w EDTA disodium salt (AR grade). External calibration was done using a commercially available total iodine standard (10 mg/L, High Purity Standards) diluted in the same matrix as the samples to the following concentrations: 0, 0.5, 1, 5, 10, 50 and 100 µg/L. An internal standard, Terbium (159 $m/z$), was added to all standards and samples at a concentration of 100 µg/L using an online mixing tee and monitored to correct for instrument drift. Duplicate analysis was done on five samples to determine relative percent differences from 0.4% to 6.4%. Spike recovery analysis was done on four samples, where a known amount of iodine was spiked into duplicate samples and recovery was 93%–107%. Serum ferritin and haemoglobin levels during the second trimester were obtained from clinical records.

### 2.4 | Statistical analyses

Statistical analyses were performed in SPSS (Version 29.0., IBM Corp). The distribution of continuous variables was assessed using Shapiro–Wilk test for normality. The distribution of supplement use by maternal characteristics were compared using the $\chi^2$ test for categorical variables and Mann–Whitney *U* test for continuous variables. The distribution of nutrient intake, guideline alignment and blood or urine nutrient levels by supplement use were compared using the $\chi^2$ test for categorical variables and Kruskal–Wallis *H* test for continuous variables, with pairwise comparisons adjusted using the Bonferroni correction for multiple tests. Folate and iron status were compared between participants who exceeded and did not exceed respective UL by Mann–Whitney *U* tests. Multivariate linear regression analysis was used to assess maternal characteristics that were associated with mean daily dose of supplemental nutrients. Maternal characteristics (predictors) were added to the model simultaneously and included age; Caucasian ethnicity, BMI; parity (reference: nulliparous); planned conception; model of antenatal care (reference: midwifery group practice); weekly household income; private health insurance, education (reference: Bachelor's degree); chronic physical condition/s; mental health condition/s; and diagnosed anaemia. Missing values for race ($n$ = 1); planned or unplanned conception ($n$ = 2); spontaneous or assisted conception ($n$ = 2); model of antenatal care ($n$ = 1); weekly household income ($n$ = 27); plasma zinc, calcium, iron and iodine ($n$ = 3); plasma folate ($n$ = 1); serum ferritin ($n$ = 69); haemoglobin ($n$ = 4) and urinary iodine ($n$ = 3) were imputed as null values.

## 3 | RESULTS

Dietary intake data were available from 129 pregnant participants. One participant was removed due to twin pregnancy and one outlier was removed due to folic acid supplement intake level of 5500 µg, resulting in 127 participants included in the current analysis (Figure 1 and Table 1). The median age was 33.7 (interquartile range [IQR]: 29.8, 35.9) years and 71.4% of participants were Caucasian. The majority of participants had a pre-pregnancy BMI within the healthy range (62.2%) and approximately one-third had prepregnancy BMI in the overweight (19.7%) or obese (13.4%) categories. The majority were nulliparous (47.2%), had a planned pregnancy (80.8%) and conceived spontaneously (93.6%). Models of antenatal care were distributed between midwifery group practice (27%), private obstetrician (23%), GP shared care (21%), specialist care clinic (16%) and midwifery hospital care (13%). The study demographic consisted of almost 80% residing in upper tertile postcodes (SEIFA), a median weekly household income of $2000 AUD, 61.4% with private health cover and >70% held a Bachelor's degree or higher. A diagnosed physical health condition was reported by more than 70% of participants, with the most common being asthma (21%), skin disease (14%), thyroid condition (11%), gastrointestinal disease (10%), low blood pressure (9%), endometriosis (9%) and endocrine disease not including diabetes mellitus or thyroid conditions (9%). A diagnosed mental health disorder was reported by 23.6% of study participants. At 28 weeks of pregnancy, 10.2% had diagnosed anaemia.

Birth onset was distributed as follows: 47.6% spontaneous labour, 30.2% induction of labour, 20.6% scheduled caesarean section and 1.6% other. Vaginal deliveries occurred in 64.3% with caesarean section delivery in 35.7% of pregnancies. Infant sex distribution was 52% female and 48% male. Median (IQR) birth weight and gestational age at delivery were 3.42 (3.19–3.78) kg and 39.1 (38.3-40.1) weeks, respectively. Three infants (2.4%) were born small for gestational age for sex, 5.5% were born preterm

**TABLE 1** Supplement use by maternal characteristics.

| | | Any supplement | | | MMN supplement | | | Individual supplement | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Total, $n$ = 127 | Yes, $n$ = 113 | No, $n$ = 14 | $p$ | Yes, $n$ = 103 | No, $n$ = 24 | $p$ | Yes, $n$ = 44 | No, $n$ = 83 | $p$ |
| Age [median (IQR), years] | 33.7 (29.8, 35.9) | 33.8 (30.1, 35.7) | 30.9 (25.8, 37.0) | 0.423 | 34.0 (30.2, 35.9) | 32.7 (25.6, 35.7) | 0.110 | 34.0 (31.3, 35.7) | 33.1 (28.7, 35.9) | 0.310 |
| Age category [%, ($n$)] | | | | **0.026**[a] | | | 0.173 | | | 0.149 |
| 20–29 | 24.4 (31) | 77.4 (24) | 22.6 (7) | | 67.7 (21) | 32.3 (10) | | 29.0 (9) | 71.0 (22) | |
| 30–33 | 26.0 (33) | 97.0 (32) | 3.0 (1) | | 87.9 (29) | 12.1 (4) | | 27.3 (9) | 72.7 (24) | |
| 34–35 | 24.4 (31) | 96.8 (30) | 3.2 (1) | | 83.9 (26) | 16.1 (5) | | 51.6 (16) | 48.4 (15) | |
| 36–46 | 25.2 (32) | 84.4 (27) | 15.6 (5) | | 84.4 (27) | 15.6 (5) | | 31.3 (10) | 68.8 (22) | |
| Race [%, ($n$)] | | | | 0.672[a] | | | 0.821[a] | | | 0.772[a] |
| Caucasian | 71.4 (90) | 86.7 (78) | 13.3 (12) | | 77.8 (70) | 22.2 (20) | | 34.4 (31) | 65.6 (59) | |
| Aboriginal or Torres Strait Islander | 0.8 (1) | 100 (1) | 0.0 (0) | | 100 (1) | 0 (0) | | 0 (0) | 100 (1) | |
| North East Asian | 2.4 (3) | 66.7 (2) | 33.3 (1) | | 66.7 (2) | 33.3 (1) | | 33.3 (1) | 66.7 (2) | |
| South Central Asian | 4.0 (5) | 100 (5) | 0.0 (0) | | 100 (5) | 0 (0) | | 60.0 (3) | 40.0 (2) | |
| South East Asian | 2.4 (3) | 100 (3) | 0.0 (0) | | 100 (3) | 0 (0) | | 33.3 (1) | 66.7 (2) | |
| Central or South American | 6.3 (8) | 100 (8) | 0.0 (0) | | 87.5 (7) | 12.5 (1) | | 50.0 (4) | 50.0 (4) | |
| Mixed or other | 12.7 (16) | 93.8 (15) | 6.3 (1) | | 87.5 (14) | 12.5 (2) | | 25.0 (4) | 75.0 (12) | |
| BMI [median (IQR), kg/m$^2$] | 23.4 (21.2, 27.2) | 23.3 (21.0, 27.3) | 24.1 (22.7, 27.7) | 0.258 | 23.2 (21.0, 27.2) | 24.9 (22.5, 28.5) | 0.116 | 23.4 (21.3, 25.3) | 23.5 (21.0, 28.9) | 0.667 |
| BMI category [%, ($n$)] | | | | 0.561[a] | | | 0.185[a] | | | 0.200[a] |
| Underweight (<18.5) | 4.7 (6) | 83.3 (5) | 16.7 (1) | | 83.3 (5) | 16.7 (1) | | 0 (0) | 100 (6) | |
| Healthy weight (18.5–24.9) | 62.2 (79) | 91.1 (72) | 8.9 (7) | | 86.1 (68) | 13.9 (11) | | 39.2 (31) | 60.8 (48) | |
| Overweight (25.0–29.9) | 19.7 (25) | 84.0 (21) | 16.0 (4) | | 68.0 (17) | 32.0 (8) | | 36.0 (9) | 64.0 (16) | |
| Obese (≥30.0) | 13.4 (17) | 88.2 (15) | 11.8 (2) | | 76.5 (13) | 23.5 (4) | | 23.5 (4) | 76.5 (13) | |
| Parity [%, ($n$)] | | | | 0.156[a] | | | 0.359[a] | | | 0.712[a] |
| 0 | 47.2 (60) | 93.3 (56) | 6.7 (4) | | 80.0 (48) | 20.0 (12) | | 36.7 (22) | 63.3 (38) | |
| 1 | 42.5 (54) | 87.0 (47) | 13.0 (7) | | 85.2 (46) | 14.8 (8) | | 35.2 (19) | 64.8 (35) | |
| 2+ | 10.2 (13) | 76.9 (10) | 23.1 (3) | | 69.2 (9) | 30.8 (4) | | 23.1 (3) | 76.9 (10) | |
| Conception planned [%, ($n$)] | | | | 0.469[a] | | | 0.246[a] | | | 0.722 |
| Yes | 80.8 (101) | 90.1 (91) | 9.9 (10) | | 83.2 (84) | 16.8 (17) | | 33.7 (34) | 66.3 (67) | |
| No | 19.2 (24) | 83.3 (20) | 16.7 (4) | | 70.8 (17) | 29.2 (7) | | 37.5 (9) | 62.5 (15) | |

TABLE 1 (Continued)

| | | Any supplement | | | MMN supplement | | | Individual supplement | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Total, $n$ = 127 | Yes, $n$ = 113 | No, $n$ = 14 | $p$ | Yes, $n$ = 103 | No, $n$ = 24 | $p$ | Yes, $n$ = 44 | No, $n$ = 83 | $p$ |
| Conception type [%, (n)] | | | | 0.596[a] | | | 1.000[a] | | | 0.450[a] |
| Spontaneous | 93.6 (117) | 88.0 (103) | 12.0 (14) | | 80.3 (94) | 19.7 (23) | | 34.2 (40) | 65.8 (77) | |
| Assisted | 6.4 (8) | 100 (8) | 0 (0) | | 87.5 (7) | 12.5 (1) | | 50.0 (4) | 50.0 (4) | |
| Model of antenatal care [%, (n)] | | | | **0.021**[a] | | | **0.001**[a] | | | 0.245 |
| GP shared care | 20.6 (26) | 92.3 (24) | 7.7 (2) | | 80.8 (21) | 19.2 (5) | | 46.2 (12) | 53.8 (14) | |
| Private obstetrician | 23.0 (29) | 100 (29) | 0 (0) | | 100 (29) | 0 (0) | | 37.9 (11) | 62.1 (18) | |
| Midwifery hospital care | 13.5 (17) | 88.2 (15) | 11.8 (2) | | 88.2 (15) | 11.8 (2) | | 41.2 (7) | 58.8 (10) | |
| Midwifery group practice | 27.0 (34) | 88.2 (30) | 11.8 (4) | | 73.5 (25) | 26.5 (9) | | 32.4 (11) | 67.6 (23) | |
| Specialist care | 15.9 (20) | 70.0 (14) | 30.0 (6) | | 60.0 (12) | 40.0 (8) | | 15.0 (3) | 85.0 (17) | |
| SEIFA tertile [%, (n)] | | | | 0.101[a] | | | 0.381[a] | | | 0.840[a] |
| Lower | 8.7 (11) | 100 (11) | 0 (0) | | 90.9 (10) | 9.1 (1) | | 27.3 (3) | 72.7 (8) | |
| Middle | 12.6 (16) | 75.0 (12) | 25.0 (4) | | 68.8 (11) | 31.3 (5) | | 31.3 (5) | 68.8 (11) | |
| Upper | 78.7 (100) | 90.0 (90) | 10.0 (10) | | 82.0 (82) | 18.0 (18) | | 36.0 (36) | 64.0 (64) | |
| Weekly income [median (IQR), $AUD] | 2000 (1353, 2588) | 2000 (1450, 2800) | 1361 (948, 2025) | **0.018** | 2000 (1442, 2900) | 1600 (1250, 2108) | 0.112 | 2000 (1263, 2450) | 1975 (1371, 2875) | 0.502 |
| Private health insurance [%, (n)] | | | | **0.001** | | | **<0.001** | | | 0.449 |
| Yes | 61.4 (78) | 96.2 (75) | 3.8 (3) | | 91.0 (71) | 9.0 (7) | | 37.2 (29) | 62.8 (49) | |
| No | 38.6 (49) | 77.6 (38) | 22.4 (11) | | 65.3 (32) | 34.7 (17) | | 30.6 (15) | 69.4 (34) | |
| Education level [%, (n)] | | | | 0.560[a] | | | 0.764[a] | | | 0.977[a] |
| No tertiary qualification | 3.1 (4) | 75.0 (3) | 25.0 (1) | | 75.0 (3) | 25.0 (1) | | 25.0 (1) | 75.0 (3) | |
| Certificate, diploma or trade | 24.4 (31) | 87.1 (27) | 12.9 (4) | | 77.4 (24) | 22.6 (7) | | 32.3 (10) | 67.7 (21) | |
| Bachelor's degree | 49.6 (63) | 88.9 (56) | 11.1 (7) | | 81.0 (51) | 19.0 (12) | | 34.9 (22) | 65.1 (41) | |
| Masters or PhD | 22.8 (29) | 93.1 (27) | 6.9 (2) | | 86.2 (25) | 13.8 (4) | | 37.9 (11) | 62.1 (18) | |
| Physical health condition[b] [%, (n)] | | | | 1.000[a] | | | 0.482 | | | 0.230 |
| Yes | 72.4 (92) | 89.1 (82) | 10.9 (10) | | 82.6 (76) | 17.4 (16) | | 31.5 (29) | 68.5 (63) | |
| No | 27.6 (35) | 88.6 (31) | 11.4 (4) | | 77.1 (27) | 22.9 (8) | | 42.9 (15) | 57.1 (20) | |

(Continues)

**TABLE 1** (Continued)

| | Total, *n* = 127 | Any supplement | | | MMN supplement | | | Individual supplement | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Yes, *n* = 113 | No, *n* = 14 | *p* | Yes, *n* = 103 | No, *n* = 24 | *p* | Yes, *n* = 44 | No, *n* = 83 | *p* |
| Mental health disorder [%, (*n*)] | | | | 1.000[a] | | | 0.721 | | | 0.863 |
| Yes | 23.6 (30) | 90.0 (27) | 10.0 (3) | | 83.3 (25) | 16.7 (5) | | 33.3 (10) | 66.7 (20) | |
| No | 76.4 (97) | 88.7 (86) | 11.3 (11) | | 80.4 (78) | 19.6 (19) | | 35.1 (34) | 64.9 (63) | |
| Diagnosed anaemia at 28 weeks [%, (*n*)] | | | | 1.000[a] | | | 1.000[a] | | | **<0.001**[a] |
| Yes | 10.2 (13) | 92.3 (12) | 7.7 (1) | | 84.6 (11) | 15.4 (2) | | 84.6 (11) | 15.4 (2) | |
| No | 89.8 (114) | 88.6 (101) | 11.4 (13) | | 80.7 (92) | 19.3 (22) | | 28.9 (33) | 71.1 (81) | |
| Diet quality (ARFS) | | | | 1.000[a] | | | 0.429 | | | 0.441 |
| Lower (8–28) | 33.1 (42) | 88.1 (37) | 11.9 (5) | | 83.3 (35) | 16.7 (7) | | 38.1 (16) | 61.9 (26) | |
| Middle (29–36) | 32.3 (41) | 90.2 (37) | 9.8 (4) | | 85.4 (35) | 14.6 (6) | | 26.8 (11) | 73.2 (30) | |
| Upper (37+) | 34.6 (44) | 88.6 (39) | 11.4 (5) | | 75.0 (33) | 25.0 (11) | | 38.4 (17) | 61.4 (27) | |
| Guideline alignment [%, (*n*)] | | | | | | | | | | |
| Grain foods ≥8.5 serves | | | | 1.000[a] | | | 0.189[a] | | | 0.346[a] |
| Yes | 0.8 (1) | 100 (1) | 0 (0) | | 0 (0) | 100 (1) | | 100 (1) | 0 (0) | |
| No | 99.2 (126) | 88.9 (112) | 11.1 (14) | | 81.7 (103) | 18.3 (23) | | 34.1 (43) | 65.9 (83) | |
| Fruit ≥2 serves | | | | 0.290 | | | 0.994 | | | 0.169 |
| Yes | 41.7 (53) | 92.5 (49) | 7.5 (4) | | 81.1 (43) | 18.9 (10) | | 41.5 (22) | 58.5 (31) | |
| No | 58.3 (74) | 86.5 (64) | 13.5 (10) | | 81.1 (60) | 18.9 (14) | | 29.7 (22) | 70.3 (52) | |
| Vegetables/legume ≥5 serves | | | | 1.000[a] | | | 0.585 | | | 0.411 |
| Yes | 25.2 (32) | 90.6 (29) | 9.4 (3) | | 84.4 (27) | 15.6 (5) | | 40.6 (13) | 59.4 (19) | |
| No | 74.8 (95) | 88.4 (84) | 11.6 (11) | | 80.0 (76) | 20.0 (19) | | 32.6 (31) | 67.4 (64) | |
| Dairy/alternative ≥2.5 serves | | | | 0.186[a] | | | 0.139[a] | | | **0.018**[a] |
| Yes | 11.0 (14) | 78.6 (11) | 21.4 (3) | | 64.3 (9) | 35.7 (5) | | 64.3 (9) | 35.7 (5) | |
| No | 89.0 (113) | 90.3 (102) | 9.7 (11) | | 83.2 (94) | 16.8 (19) | | 31.0 (35) | 69.0 (78) | |

**TABLE 1** (Continued)

| | Total, $n = 127$ | Any supplement | | | MMN supplement | | | Individual supplement | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Yes, $n = 113$ | No, $n = 14$ | $p$ | Yes, $n = 103$ | No, $n = 24$ | $p$ | Yes, $n = 44$ | No, $n = 83$ | $p$ |
| Meat/vegetarian alternative ≥3.5 serves | | | | 0.124[a] | | | **0.013[a]** | | | 0.971 |
| Yes | 15.7 (20) | 100 (20) | 0 (0) | | 100 (20) | 0 (0) | | 35.0 (7) | 65.0 (13) | |
| No | 84.3 (107) | 86.9 (93) | 13.1 (14) | | 77.6 (83) | 22.4 (24) | | 34.6 (37) | 65.4 (70) | |

*Note*: Bold values indicate statistical significance. Percentages refer to proportion of participants supplementing or not supplementing by each maternal characteristic (within rows). Here, 26.8% of participants reported both MMN and individual supplement use; therefore, numbers between supplement groups are not mutually exclusive.

Abbreviations: ARFS, Australian Recommended Food Score; BMI, body mass index; GDM, gestational diabetes mellitus; GP, general practitioner; IQR, interquartile range; MMN, multiple micronutrient; SEIFA, Socioeconomic Indexes for Areas.

[a]Fisher's exact test (where at least one cell had expected count <5) was used for categorical variables. Mann–Whitney *U* test was used for continuous variables.

[b]Physical health condition includes any of the following: asthma, other respiratory disease, hypertension, hypotension, heart disease, kidney disease, blood coagulation disorder, diabetes mellitus (T1DM, T2DM, GDM), thyroid condition, other endocrine disorder, endometriosis and gastrointestinal disorder including coeliac, neurological disorder, musculoskeletal disorder, sleep disorder, autoimmune disorder, inherited conditions, cancer, skin disease and chronic infectious disease.

(<37 weeks' gestation) and 10.4% were admitted to the neonatal intensive care unit or special care nursery.

Supplement use at 28 weeks' gestation was reported by 89% of participants, of whom 91% reported taking a MMN supplement and 39% reported taking individual supplement/s (26.8% used both a MMN supplement and individual supplement/s) (Figure 2). The most common MMN supplement used was Elevit, reported by 45% of all supplement users, and the most common individual nutrient supplements were iron (with or without vitamin C) and folic acid, reported by 27% and 14% of all supplement users, respectively.

Participants who used any supplement in pregnancy were more likely to be aged ≥30 years, be receiving private obstetric care, have a higher weekly income and have private health insurance (Table 1). Participants who used a MMN supplement in pregnancy were more likely to be receiving private obstetric care, have private health insurance and have greater dietary alignment to meat/vegetarian alternatives recommendations. Participants who used an individual supplement/s in pregnancy were more likely to have diagnosed anaemia at 28 weeks' gestation and report greater dietary alignment to the dairy/alternatives category.

Alignment with nutrient intake targets for folate, zinc, iodine and iron differed among the categories of supplement users (Tables 2 and 3). Among those taking a MMN supplement with any individual supplement/s, MMN supplement only, individual folic acid only ($n = 8$) and no supplement, the folate EAR was met by 100%, 98.6%, 87.5% and 14.3% of participants, respectively. Among those taking MMN with any individual supplement/s, MMN supplement only, individual iron only ($n = 4$) and no supplement, the iron EAR was met by 97.1%, 50.7%, 100% and 0%, of participants, respectively. For zinc and iodine, proportions meeting respective EARs were 100%, >95% and 28.6%–42.9% among those taking a MMN with any individual supplement/s, MMN supplement only and no supplement, respectively (no participants took zinc or iodine as an individual supplement only). There were no differences in guideline alignment for calcium between the categories of supplement users.

For supplemental folic acid, seven participants (5.5%) exceeded the UL, of which six were taking MMN with any individual supplement/s. For iron, almost 50% of participants exceeded the UL, which was driven by those taking a MMN with any individual supplement/s or MMN supplement alone. UL for zinc, calcium and iodine intakes were not exceeded by any participant (data not shown).

Total intakes of folate, zinc, iodine and iron differed between the different supplement user groups. For folate, zinc and iodine, MMN supplement users (with or without individual supplement) had significantly higher intakes than non-MMN supplement users. Combined MMN and any individual supplement/s users had significantly higher intakes of iron than the other three groups. Iron intake was also higher among MMN supplement only versus no supplement group. Among those supplementing with individual iron only ($n = 4$), total iron intake was significantly higher than MMN supplement-only users. Total calcium intake did not differ between supplement user groups by adjusted pairwise comparisons; there

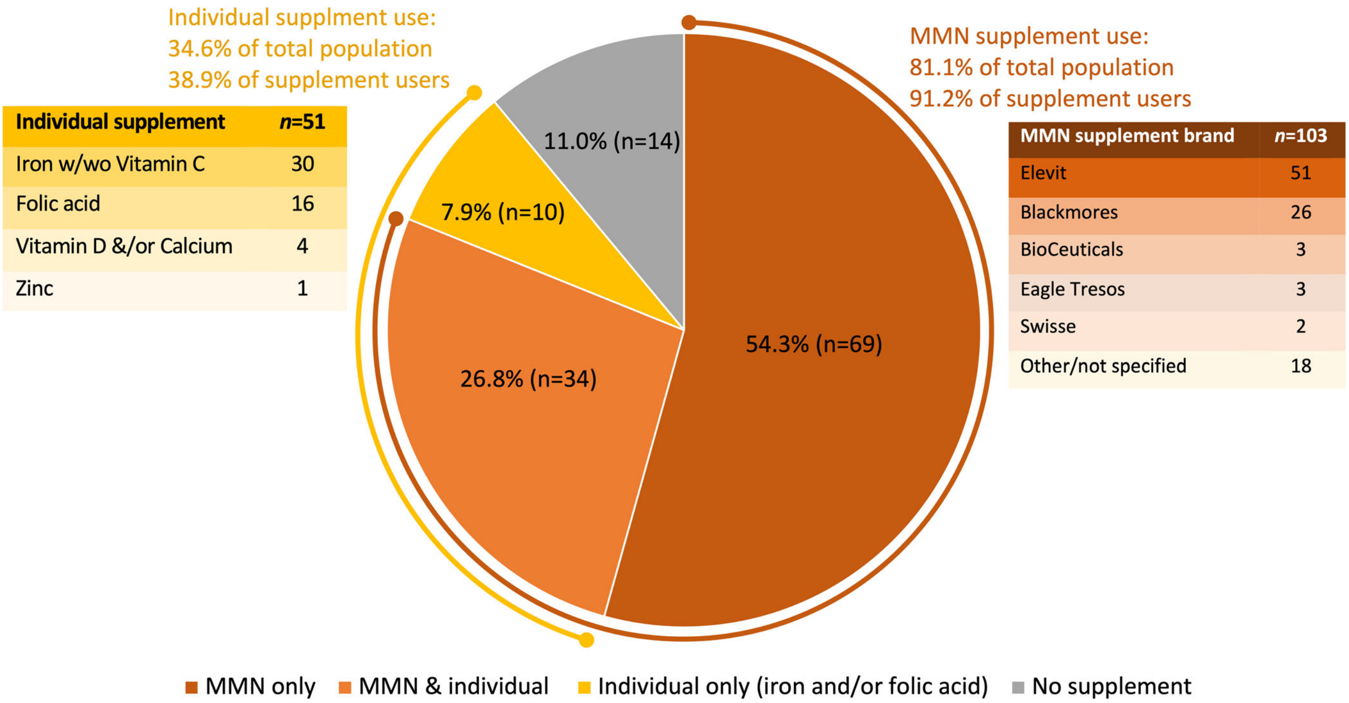


**FIGURE 2** Proportion of dietary supplement types taken at 28 weeks' pregnancy ($n = 127$). Individual supplement use was reported by $n = 44$, of which $n = 7$ reported two different individual supplements. Of the $n = 10$ participants that reported taking an individual supplement/s only, $n = 6$ reported folic acid, $n = 2$ reported iron and $n = 2$ reported both folic acid and iron. MMN, multiple micronutrient.

was a trend for higher intakes in combined MMN and individual supplement users compared with MMN supplement-only users ($p = 0.056$) and nonusers ($p = 0.072$).

Biological nutrient status by supplement use differed for folate only, with a lower plasma concentration in nonsupplement users compared with MMN users. There was no difference in plasma folate levels between those taking an individual folic acid supplement ($n = 8$) versus taking a MMN supplement only ($n = 69$). Plasma folate levels were significantly higher among those who exceeded the UL for folic acid versus those that did not (median, IQR: 20.2, 17.9–30.2 vs. 17.2, 11.5–20.7 µg/L, respectively, $p = 0.021$). Likewise, plasma iron levels tended to be higher (median, IQR: 911, 693–1185 vs. 760, 552–1095 µg/L, $p = 0.063$), albeit there was no difference in serum ferritin (median, IQR: 20.0, 10.0–36.0 vs. 13.0, 8.0–29.0 µg/L, $p = 0.186$) and haemoglobin (median, IQR: 119, 111–123 vs. 115, 110–122 g/L, $p = 0.355$) levels between those who exceeded the UL for elemental iron versus those that did not, respectively. Mild iodine insufficiency (defined as urinary iodine concentration <150 µg/L) was apparent in 44% of study participants but a $\chi^2$ test revealed no significant differences in this proportion between MMN users and nonusers ($p = 0.281$).

Figure 3 shows the proportion of total micronutrient intakes provided from food versus nutrient supplements for folate, calcium, iodine, zinc and iron. The majority of the total intakes for folate (as DFE) (74%), iodine (57%), zinc (52%) and iron (73%) came from nutrient supplements, whereas only 12% of total calcium intake came from nutrient supplements. Median zinc intake from diet alone was sufficient to meet the EAR (and slightly exceed it) and dietary calcium intake was 85% of the EAR. On the other hand, median folate, iodine and iron intakes from dietary sources alone was only 58%, 71% and 43% of respective EARs. Aligned with these data, when considering dietary sources only, the proportion of participants who met zinc and calcium EARs was 63% and 30%, respectively, whereas folate, iodine and iron EARs were met by only 4.7%, 16.5% and 0.8% of participants, respectively.

A multivariate linear regression analysis was performed to determine whether mean daily dose of supplemental nutrients can be predicted based on certain maternal characteristics, including age; Caucasian ethnicity, BMI; parity; planned conception; model of antenatal care; weekly household income; private health insurance, education level; physical health condition; mental health disorder; and diagnosed anaemia (Table 4). This model accounted for 32.9% of the variance associated with supplemental folic acid ($F_{18,80} = 2.179$; $p = 0.01$); 27.2% for supplemental zinc ($F_{18,80} = 1.659$; $p = 0.065$); 24.3% for supplemental calcium ($F_{18,80} = 1.423$; $p = 0.144$); 31.2% for supplemental iodine ($F_{18,80} = 2.020$; $p = 0.018$); and 46.3% for supplemental iron ($F_{18,80} = 3.824$; $p < 0.001$). Private health insurance was the strongest positive predictor of supplemental folic acid, followed by GP shared care and mental health condition. Parity ≥ 2 was a significant negative predictor of supplemental folic acid. Private obstetric care was the only significant positive predictor of supplemental zinc and calcium. Private health insurance was the strongest positive predictor of supplemental iodine, followed by private obstetric care and GP shared care. Midwifery hospital care,

**TABLE 2** Nutrient guideline alignment, total micronutrient intake and biochemical nutrient status by type of supplement use.

| | Total<br>*n* = 127 | MMN supplement and any individual supplement<br>*n* = 34 | MMN supplement only<br>*n* = 69 | Individual supplement only (iron and/or folic acid)<br>*n* = 10 | No supplement<br>*n* = 14 | *p* |
|---|---|---|---|---|---|---|
| Folate (as DFEs) | | | | | | |
| Meet EAR (520 µg/d) [%, (*n*)] | | | | | | **<0.001** |
| Yes | 88.2 (112) | 100 (34) | 98.6 (68) | 80.0 (8) | 14.3 (2) | |
| No | 11.8 (15) | 0 (0) | 1.4 (1) | 20.0 (2) | 85.7 (12) | |
| Exceed UL* (1000 µg/d) [%, (*n*)] | | | | | | **0.011** |
| Yes | 5.5 (7) | 17.6 (6) | 1.4 (1) | 0 (0) | 0 (0) | |
| No | 94.5 (120) | 82.4 (28) | 98.6 (68) | 100 (10) | 100 (14) | |
| Total intake [median (IQR), µg/d] | 1126 (942, 1610) | 1572 (1124, 1814)[a] | 1176 (1029, 1603)[a] | 955 (520, 1054)[b] | 282 (228, 394)[b] | **<0.001** |
| Plasma levels [median (IQR), µg/L] | 17.4 (12.1, 20.8) | 18.2 (15.5, 21.9)[a] | 17.4 (12.9, 20.7)[a] | 13.5 (9.6, 21.6)[a,b] | 9.0 (6.5, 18.8)[b] | **0.015** |
| Zinc | | | | | | |
| Meet EAR (9 mg/d) [%, (*n*)] | | | | | | **<0.001** |
| Yes | 91.3 (116) | 100 (34) | 97.1 (67) | 90.0 (9) | 42.9 (6) | |
| No | 8.7 (11) | 0 (0) | 2.9 (2) | 10.0 (1) | 57.1 (8) | |
| Total intake [median (IQR), mg/d] | 19.8 (15.5, 22.3) | 21.0 (19.4, 25.4)[a] | 20.2 (17.5, 22.5)[a] | 10.5 (10.0, 12.1)[b] | 8.1 (6.9, 14.1)[b] | **<0.001** |
| Plasma levels [median (IQR), µg/L] | 586 (520, 645) | 602 (526, 663) | 595 (519, 643) | 545 (519, 629) | 558 (473, 679) | 0.609 |
| Calcium | | | | | | |
| Meet EAR (840 mg/d) [%, (*n*)] | | | | | | 0.119 |
| Yes | 42.5 (54) | 55.9 (19) | 36.2 (25) | 60.0 (6) | 28.6 (4) | |
| No | 57.5 (73) | 44.1 (15) | 63.8 (44) | 40.0 (4) | 71.4 (10) | |
| Total intake [median (IQR), mg/d] | 785 (574, 1001) | 850 (663, 1367) | 755 (551, 909) | 967 (713, 1202) | 634 (371, 1054) | **0.011** |
| Plasma levels [median (IQR), µg/L] | 45,918 (44,642, 47,533) | 46,501 (45,258, 48,161) | 45,769 (44,294, 47,338) | 45,276 (44,583, 49,110) | 46,862 (44,092, 47,658) | 0.342 |
| Iodine | | | | | | |
| Meet with EAR (160 µg/d) [%, (*n*)] | | | | | | **<0.001** |
| Yes | 83.5 (106) | 100 (34) | 95.7 (66) | 20.0 (2) | 28.6 (4) | |
| No | 16.5 (21) | 0 (0) | 4.3 (3) | 80.0 (8) | 71.4 (10) | |

(Continues)

**TABLE 2** (Continued)

| | Total $n = 127$ | MMN supplement and any individual supplement $n = 34$ | MMN supplement only $n = 69$ | Individual supplement only (iron and/or folic acid) $n = 10$ | No supplement $n = 14$ | *p* |
|---|---|---|---|---|---|---|
| Total intake [median (IQR), µg/d] | 279 (213, 337) | 338 (294, 386)[a] | 288 (241, 329)[a] | 126 (111, 162)[b] | 97.0 (72.0, 171)[b] | **<0.001** |
| Plasma levels [median (IQR), µg/L] | 91.9 (82.9, 105.7) | 97.4 (88.2, 114) | 90.7 (80.7, 103) | 96.5 (90.2, 101) | 88.0 (75.5, 102) | 0.067 |
| Urine levels [median (IQR), µg/L] | 161 (100, 272) | 158 (79.5, 278) | 171 (110, 285) | 131 (80.1, 229) | 180 (103, 252) | 0.706 |
| Iron | | | | | | |
| Meet EAR (22 mg/d) [%, (*n*)] | | | | | | **<0.001** |
| Yes | 56.7 (72) | 97.1 (33) | 50.7 (35) | 40.0 (4) | 0 (0) | |
| No | 43.3 (55) | 2.9 (1) | 49.3 (34) | 60.0 (6) | 100 (14) | |
| Exceed UL (45 mg/d) [%, (*n*)] | | | | | | **<0.001** |
| Yes | 49.6 (63) | 91.2 (31) | 42.0 (29) | 30.0 (3) | 0 (0) | |
| No | 50.4 (64) | 8.8 (3) | 58.0 (40) | 70.0 (7) | 100 (14) | |
| Total intake [median (IQR), mg/d] | 37.3 (17.3, 74.2) | 121 (70.5, 148)[a] | 22.4 (18.8, 66.2)[b] | 11.7 (8.9, 112)[b,c] | 8.1 (6.8, 10.3)[c] | **<0.001** |
| Plasma levels [median (IQR), µg/L] | 867 (657, 1145) | 858 (712, 1213) | 901 (593, 1145) | 766 (731, 1086) | 740 (471, 1111) | 0.537 |
| Serum ferritin[#] [median (IQR), µg/L] | 17.5 (10.0, 35.3) | 19.0 (10.0, 35.0) | 19.5 (9.8, 36.0) | 16.0 (10.0, 29.0) | 9.0 (5.3, 57.0) | 0.774 |
| Haemoglobin [median (IQR), g/L] | 117 (110, 123) | 116 (110, 123) | 117 (112, 123) | 120 (113, 124) | 116 (107, 123) | 0.936 |

*Note*: Bold values indicate statistical significance. Percentages refer to proportion of participants that met or exceeded relevant nutrient guidelines by type of supplement use (within columns). Fisher's Exact test was used for categorical variables. Kruskal–Wallis one-way ANOVA with Bonferroni correction for multiple pairwise comparisons was used for continuous variables. Different letters (a, b, c) denote statistical difference between supplement user categories.

Abbreviations: ANOVA, analysis of variance; DFE, dietary folate equivalent; EAR, estimated average requirement; IQR, interquartile range; MMN, multiple micronutrient; UL, upper level of intake.

*UL comparison includes folic acid from supplements only.

[#]Serum ferritin total $n = 58$; MMN supplement and any individual supplement $n = 23$; MMN supplement only $n = 26$; individual supplement only $n = 5$; no supplement $n = 4$.

**TABLE 3** Nutrient guideline alignment, total micronutrient intake and biochemical nutrient status by MMN supplement only versus individual folic acid and/or iron supplement only.

| | MMN supplement only | Individual folic acid and/or iron supplement only | *p* |
|---|---|---|---|
| Folate (as DFEs) | *n* = 69 | *n* = 8 | |
| Meet EAR (520 µg/d) [%, (*n*)] | | | 0.198 |
| Yes | 98.6 (68) | 87.5 (7) | |
| No | 1.4 (1) | 12.5 (1) | |
| Exceed UL* (1000 µg/d) [%, (*n*)] | | | 1.000 |
| Yes | 1.4 (1) | 0 (0) | |
| No | 98.6 (68) | 100 (8) | |
| Total intake [median (IQR), µg/d] | 1176 (1029, 1603) | 981 (667, 1078) | **0.006** |
| Plasma levels [median (IQR), µg/L] | 17.4 (12.9, 20.7) | 13.5 (9.5, 21.3) | 0.275 |
| Iron | *n* = 69 | *n* = 4 | |
| Meet EAR (22 mg/d) [%, (*n*)] | | | 0.118 |
| Yes | 50.7 (35) | 100 (4) | |
| No | 49.3 (34) | 0 (0) | |
| Exceed UL (45 mg/d) [%, (*n*)] | | | 0.313 |
| Yes | 42.0 (29) | 75.0 (3) | |
| No | 58.0 (40) | 25.0 (1) | |
| Total intake [median (IQR), mg/d] | 22.4 (18.8, 66.2) | 112 (45.2, 130) | **0.012** |
| Plasma levels [median (IQR), µg/L] | 901 (593, 1145) | 870 (759, 1033) | 0.921 |
| Haemoglobin [median (IQR), g/L] | 117 (112, 122) | 117 (112, 124) | 0.939 |

*Note*: Percentages refer to proportion of participants that met or exceeded relevant nutrient guideline by MMN supplement use only and by individual folic acid or iron supplement use only (within columns). Of the *n* = 10 participants that reported taking individual supplement/s only, *n* = 2 took both folic acid and iron, and were therefore included in both folate and iron comparisons. Fisher's exact test was used for categorical variables. Mann–Whitney *U* test used for continuous variables.

Abbreviations: DFE, dietary folate equivalent; EAR, estimated average requirement; MMN, multiple micronutrient; UL, upper level of intake.

*UL comparison includes folic acid from supplements only. N.B.: due to few available records for serum ferritin (i.e., *n* = 26 for MMN supplement only and *n* = 3 for individual iron supplement only), these data were not included in this analysis.

GP shared care, private obstetric care, diagnosed anaemia and private health insurance were all significant positive predictors of supplemental iron.

## 4 | DISCUSSION

The current study found that nine in 10 participants were taking at least one dietary supplement at 28 weeks' pregnancy, of whom two in three were taking a MMN supplement only, one in three were taking a MMN supplement and an individual supplement/s, and just under one in 10 were taking individual supplement/s only. Current findings suggest that MMN supplementation is influenced by variables associated with higher income, including receiving private obstetric care, holding private health insurance and higher dietary guideline alignment with meat/vegetarian alternatives. Higher mean daily dose of supplemental zinc, calcium, iodine and iron were all predicted by private obstetric care compared with the reference category, midwifery group practice. Holding private health insurance and GP shared care also independently predicted higher daily doses of supplemental folic acid, iodine and iron.

High reported levels of MMN supplement use are consistent with previous Australian studies, where ~90% of supplement users reported taking an MMN supplement in the second or third trimester (Livock et al., 2017; Malek et al., 2018; Shand et al., 2016). Among those taking a MMN supplement with or without an individual supplement, there was >94% alignment with folate, zinc and iodine EARs. For iron, 97% met the EAR if supplementing with MMN and any individual supplement and 50% met the EAR if supplementing with MMN only. The proportion of participants meeting the calcium EAR did not differ between supplement user categories. In agreement, total intakes of folate, zinc, iodine and iron came predominantly from supplementation, whereas for calcium, only 12% of total intake came from supplementation. Median zinc and

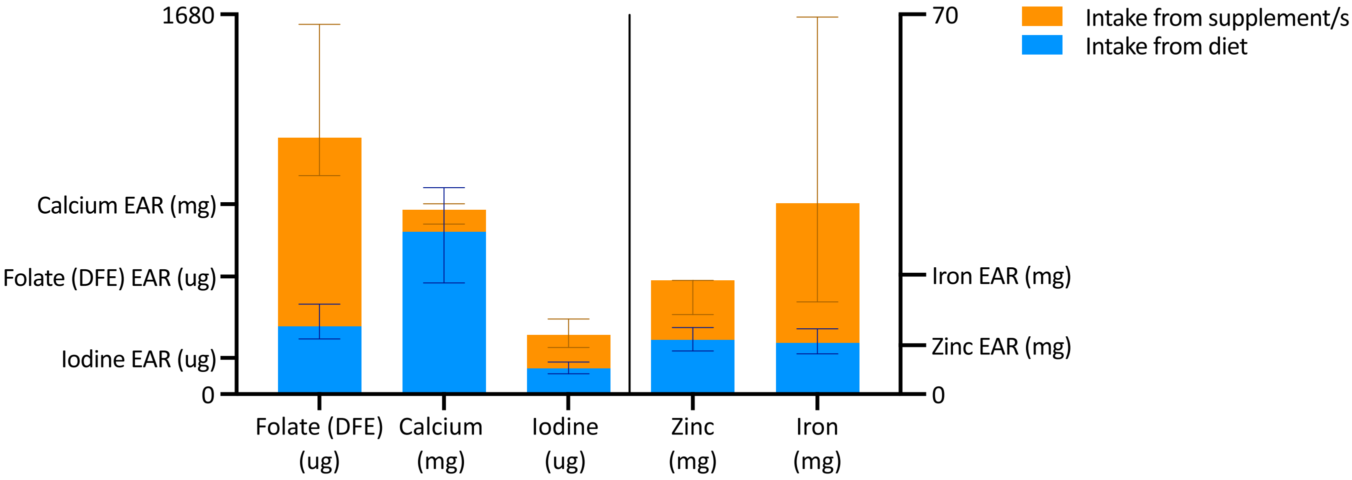


**FIGURE 3** Proportion of nutrient intake per day (medians, IQR) from diet and supplementation at 28 weeks' pregnancy. DFE, dietary folate equivalents; EAR, estimated average requirement; IQR, interquartile range. Daily intake from supplements (median, IQR, percentage relative to total intake): DFE: 835, 668–1336 µg (74%); calcium: 100, 35.7–125 mg (12%); iodine: 150, 94–220 µg (57%); zinc: 11, 4.7–11 mg (52%); iron: 25.7, 7.5–60 mg (73%).

calcium intakes from diet alone closely aligned with respective EARs, but for folate, iodine and iron, EAR alignment was achieved (and well exceeded) only when supplemental sources were considered. Among participants who were not taking any supplement, proportions meeting EARs for folate and iron were alarmingly low, revealing significant reliance on supplementation to meet some nutritional needs in second trimester.

We did not capture information about the recommendations provided by healthcare providers, but studies have consistently reported that pregnant people are strongly motivated to follow the advice of healthcare providers (Malek et al., 2018). In a southeast Queensland study, pregnant people reported doctors (49.1%) as their biggest influence on supplement use, followed by family (15.2%), their own knowledge/research (11.8%), midwives (8.6%) and the media (5.7%) (McAlpine et al., 2020). In the current study, we cannot rule out a confounding influence of one's own knowledge (or lack thereof), rather than model of antenatal care per se, on high MMN supplement use and supplement dosages in pregnancy. An older Melbourne study reported that MMN supplementation during pregnancy was predominantly 'self-prescribed' (31%), with GP recommendations coming a close second (27%) and hospital doctors influencing only 7% of MMN supplement users; albeit MMN supplement use was reported by only 35% of the total study population (Forster et al., 2009). Future studies should examine contemporary views of both healthcare providers and pregnant people with respect to clinical recommendations and its influence on supplementation practices.

A common motivating factor for taking supplements in pregnancy is for 'peace of mind' that nutritional needs are being met and as a more efficient way of obtaining required nutrients compared to food (Malek et al., 2018). In this prior study, supplement users (of whom 83% took a MMN supplement during pregnancy) had low confidence that their nutritional needs were being met; they suspected low intakes of nutritionally dense foods such as green leafy vegetables or red meat, and/or lacked the knowledge to decide whether dietary intake was adequate (Malek et al., 2018). This supported previous work in nonpregnant females, where supplement users felt strongly that 'poor food quality' and 'problems eating a balanced diet' facilitate supplement use (Conner et al., 2001). Interestingly, nonalignment with fruits and vegetables was not associated with greater supplement use and nonalignment with meat/vegetarian alternative recommendations was associated with lower MMN supplementation. In a previous Australian study, overall supplement use in early pregnancy was associated with the consumption of a folate-rich diet and an annual household income >$100,000 AUD (Livock et al., 2017). With the exception of iron, high overall supplement use in pregnancy among a mostly affluent population appears to have little to do with compensating for poor diet quality and/or specific nutrient deficiencies but may reflect education and/or financial capacity to take supplements as a pregnancy safeguard.

In a meta-analyses of studies conducted in high-income countries, MMN supplement use was associated with a reduced risk of adverse birth outcomes (small for gestational age and some congenital anomalies), but almost all studies compared MMN supplement users with nonsupplement users and MMN supplementation was restricted predominantly to the periconceptional period (Wolf et al., 2017). It is therefore unknown whether MMN supplementation offers benefits that are superior to folic acid and iodine alone, and other micronutrients when indicated (e.g., iron), nor when taken beyond the first trimester. Although research is limited, MMN supplementation in high-income countries has been associated with an increased risk of developing gestational diabetes and increased offspring adiposity (Petry et al., 2020), which may be attributed to high doses of elemental iron (Petry, 2022), and MMN supplementation >5 times per week has been associated with an increased risk of autism spectrum disorder in offspring (Raghavan

**TABLE 4** Multivariate linear regression analysis for effect of maternal characteristics on mean daily dose of supplemental nutrients.

| | Estimate | Lower 95% CI | Upper 95% CI | *p* |
|---|---|---|---|---|
| Supplemental folic acid (μg), $F_{18,80} = 2.179$, $P = 0.01$, $R^2 = 0.329$ | | | | |
| Age (years) | 1.9 | −12.6 | 16.3 | 0.798 |
| Caucasian ethnicity (Yes) | −154 | −322 | 13.6 | 0.071 |
| BMI (kg/m²) | −0.8 | −14.8 | 13.2 | 0.909 |
| Parity (reference: 0) | | | | |
| 1 | −73.3 | −199 | 52.6 | 0.250 |
| 2+ | −278 | −542 | −13.7 | **0.040** |
| Conception planned (Yes) | 150 | −13.5 | 314 | 0.072 |
| Model of antenatal care (reference: midwifery group practice) | | | | |
| GP shared care | 214 | 35.7 | 393 | **0.019** |
| Private obstetrician | 186 | −18.7 | 391 | 0.074 |
| Midwifery hospital care | 105 | −105 | 316 | 0.322 |
| Specialist care | −42.0 | −254 | 170 | 0.695 |
| Weekly income ($AUD) | 0.0 | −0.1 | 0.1 | 0.785 |
| Private health insurance (Yes) | 188 | 37.9 | 339 | **0.015** |
| Education level (reference: Bachelor's degree) | | | | |
| No tertiary qualification | 246 | −80.5 | 572 | 0.138 |
| Certificate, diploma or trade | 27.2 | −156 | 211 | 0.768 |
| Masters or PhD | −39.4 | −191 | 112 | 0.607 |
| Physical health condition (Yes) | −36.8 | −180 | 106 | 0.610 |
| Mental health disorder (Yes) | 170 | 17.5 | 322 | **0.029** |
| Diagnosed anaemia at 28 weeks (Yes) | 56.4 | −157 | 270 | 0.600 |
| Supplemental zinc (mg), $F_{18,80} = 1.659$; $P = 0.065$, $R^2 = 0.272$ | | | | |
| Age (years) | 0.1 | −0.2 | 0.3 | 0.444 |
| Caucasian ethnicity (Yes) | −1.9 | −4.8 | 1.0 | 0.186 |
| BMI (kg/m²) | −0.2 | −0.4 | 0.1 | 0.120 |
| Parity (reference: 0) | | | | |
| 1 | 0.1 | −2.0 | 2.3 | 0.910 |
| 2+ | −3.9 | −8.4 | 0.6 | 0.091 |
| Conception planned (Yes) | 1.6 | −1.3 | 4.4 | 0.273 |
| Model of antenatal care (reference: midwifery group practice) | | | | |
| GP shared care | 2.8 | −0.3 | 5.8 | 0.077 |
| Private obstetrician | 4.0 | 0.5 | 7.5 | **0.027** |
| Midwifery hospital care | 1.9 | −1.8 | 5.5 | 0.308 |
| Specialist care | −1.0 | −4.6 | 2.7 | 0.598 |
| Weekly income ($AUD) | 0.0 | 0.0 | 0.0 | 0.244 |
| Private health insurance (Yes) | 2.2 | −0.4 | 4.8 | 0.098 |

(Continues)

**TABLE 4** (Continued)

| | Estimate | Lower 95% CI | Upper 95% CI | *p* |
|---|---|---|---|---|
| Education level (reference: Bachelor's degree) | | | | |
| No tertiary qualification | 5.3 | −0.3 | 10.9 | 0.065 |
| Certificate, diploma or trade | 2.1 | −1.0 | 5.3 | 0.182 |
| Masters or PhD | −0.4 | −3.1 | 2.2 | 0.732 |
| Physical health condition (Yes) | −0.7 | −3.2 | 1.8 | 0.571 |
| Mental health disorder (Yes) | 2.1 | −0.5 | 4.7 | 0.116 |
| Diagnosed anaemia at 28 weeks (Yes) | −0.2 | −3.8 | 3.5 | 0.929 |
| Supplemental Calcium (mg), $F_{18,80} = 1.423$; $P = 0.144$, $R^2 = 0.243$ | | | | |
| Age (years) | 4.3 | −2.3 | 11.0 | 0.200 |
| Caucasian ethnicity (Yes) | −30.7 | −108 | 46.4 | 0.431 |
| BMI (kg/m2) | −1.9 | −8.3 | 4.6 | 0.566 |
| Parity (reference: 0) | | | | |
| 1 | 16.5 | −41.4 | 74.3 | 0.573 |
| 2+ | −53.7 | −175 | 67.8 | 0.382 |
| Conception planned (Yes) | −7.5 | −82.8 | 67.8 | 0.843 |
| Model of antenatal care (reference: midwifery group practice) | | | | |
| GP shared care | 66.5 | −15.7 | 149 | 0.111 |
| Private obstetrician | 158 | 64.1 | 252 | **0.001** |
| Midwifery hospital care | 8.4 | −88.3 | 105 | 0.862 |
| Specialist care | 37.3 | −60.3 | 135 | 0.449 |
| Weekly income ($AUD) | 0.0 | −0.1 | 0.0 | 0.105 |
| Private health insurance (Yes) | 19.1 | −50.1 | 88.3 | 0.585 |
| Education level (reference: Bachelor's degree) | | | | |
| No tertiary qualification | 19.7 | −130 | 170 | 0.794 |
| Certificate, diploma or trade | 64.2 | −20.2 | 149 | 0.134 |
| Masters or PhD | 44.6 | −25.1 | 114 | 0.206 |
| Physical health condition (Yes) | 24.1 | −41.6 | 89.8 | 0.468 |
| Mental health disorder (Yes) | 9.4 | −60.7 | 79.4 | 0.791 |
| Diagnosed anaemia at 28 weeks (Yes) | 39.6 | −58.6 | 138 | 0.425 |
| Supplemental Iodine (µg), $F_{18,80} = 2.020$; $P = 0.018$, $R^2 = 0.312$ | | | | |
| Age (years) | 1.3 | −3.0 | 5.6 | 0.552 |
| Caucasian ethnicity (Yes) | −40.8 | −90.6 | 9.1 | 0.108 |
| BMI (kg/m2) | −1.7 | −5.8 | 2.5 | 0.428 |
| Parity (reference: 0) | | | | |
| 1 | −5.6 | −43.1 | 31.8 | 0.766 |
| 2+ | −65.6 | −144.2 | 13.0 | 0.101 |
| Conception planned (Yes) | 37.6 | −11.1 | 86.4 | 0.128 |
| Model of antenatal care (reference: midwifery group practice) | | | | |

**TABLE 4** (Continued)

| | Estimate | Lower 95% CI | Upper 95% CI | *p* |
|---|---|---|---|---|
| GP shared care | 56.4 | 3.2 | 110 | **0.038** |
| Private obstetrician | 70.6 | 9.6 | 131 | **0.024** |
| Midwifery hospital care | 36.7 | −25.9 | 99.4 | 0.246 |
| Specialist care | −21.4 | −84.6 | 41.7 | 0.501 |
| Weekly income ($AUD) | 0.0 | 0.0 | 0.0 | 0.158 |
| Private health insurance (Yes) | 54.6 | 9.8 | 99.3 | **0.018** |
| Education level (reference: Bachelor's degree) | | | | |
| No tertiary qualification | 74.9 | −22.1 | 172 | 0.128 |
| Certificate, diploma or trade | 17.7 | −36.9 | 72.3 | 0.520 |
| Masters or PhD | −22.0 | −67.0 | 23.1 | 0.335 |
| Physical health condition (Yes) | −6.3 | −48.8 | 36.3 | 0.770 |
| Mental health disorder (Yes) | 44.1 | −1.2 | 89.4 | **0.056** |
| Diagnosed anaemia at 28 weeks (Yes) | −3.1 | −66.6 | 60.4 | 0.923 |
| Supplemental Iron (mg), $F_{18,80} = 3.824$; $P < 0.001$, $R^2 = 0.463$ | | | | |
| Age (years) | −1.0 | −3.0 | 1.0 | 0.324 |
| Caucasian ethnicity (Yes) | −18.3 | −41.9 | 5.2 | 0.126 |
| BMI (kg/m2) | 0.3 | −1.7 | 2.2 | 0.799 |
| Parity (reference: 0) | | | | |
| 1 | −0.6 | −18.3 | 17.1 | 0.946 |
| 2+ | −5.3 | −42.4 | 31.9 | 0.779 |
| Conception planned (Yes) | 4.5 | −18.5 | 27.6 | 0.697 |
| Model of antenatal care (reference: midwifery group practice) | | | | |
| GP shared care | 55.8 | 30.7 | 81.0 | **<0.001** |
| Private obstetrician | 37.9 | 9.1 | 66.7 | **0.011** |
| Midwifery hospital care | 57.1 | 27.5 | 86.7 | **<0.001** |
| Specialist care | 2.5 | −27.3 | 32.4 | 0.867 |
| Weekly income ($AUD) | 0.0 | 0.0 | 0.0 | 0.412 |
| Private health insurance (Yes) | 30.4 | 9.2 | 51.6 | **0.005** |
| Education level (reference: Bachelor's degree) | | | | |
| No tertiary qualification | 40.1 | −5.7 | 86.0 | 0.085 |
| Certificate, diploma or trade | 7.8 | −18.0 | 33.6 | 0.551 |
| Masters or PhD | −10.3 | −31.6 | 11.0 | 0.338 |
| Physical health condition (Yes) | −8.9 | −29.1 | 11.2 | 0.378 |
| Mental health disorder (Yes) | 8.8 | −12.6 | 30.2 | 0.416 |
| Diagnosed anaemia at 28 weeks (Yes) | 58.2 | 28.2 | 88.3 | **<0.001** |

*Note*: Estimates (unstandardized coefficients) refer to how much the mean daily dose of supplemental nutrient varied by each maternal characteristic when all other characteristics were held constant.

Abbreviations: BMI, body mass index; CI, confidence interval; GP, general practitioner.

et al., 2018). Despite this, there is the common belief that supplements are safe to take during pregnancy, even if one's diet is nutritionally adequate, and that excess nutrients are simply excreted by the body (Malek et al., 2018).

In the current study, the UL for folic acid of 1000 µg/day, was exceeded by 5.5% of participants, of whom all were taking an Elevit MMN supplement combined with either an individual 400 µg folic acid supplement or a second MMN supplement. Although the recommended UL includes folic acid from both fortified foods and supplements, comparisons were made using supplemental folic acid only (folic acid fortification was not captured separately to natural folates in food); this underestimates the prevalence exceeding the folic acid UL in the current study and might explain higher rates previously reported (18% in second trimester) (Livock et al., 2017). In countries with mandatory fortification programs, exceeding the UL for folic acid is reported frequently among supplement users of childbearing age (Ledowsky et al., 2022). Although the recommendation of first trimester folic acid supplementation is well known for prevention of neural tube defects (De-Regil et al., 2015), there is evidence that exceeding the UL during the periconceptional period may decrease birth length (Pastor-Valero et al., 2011) and negatively affect child cognitive development at 4–5 years of age (Valera-Gran et al., 2017). Recent evidence also suggests that exceeding the UL for folic acid increases the risk of childhood cancer in pregnancies complicated with maternal epilepsy (Vegrim et al., 2022). Folic acid supplementation during late pregnancy (>30 weeks) has also been associated with an increased risk of childhood asthma, albeit the effect of dose was not evaluated (Whitrow et al., 2009). Beyond the first trimester, supplementation at 400 µg per day may yield positive effects on child cognitive development (McNulty et al., 2019), but the effects of high folic acid doses are mostly unknown and should be avoided unless medically indicated.

Among those exceeding the UL for folic acid, median plasma folate levels were significantly higher at >20 µg/L versus 17 µg/L in participants who did not surpass the UL. Higher circulating folate levels in second and third trimesters have been associated with reduced birthweight (Takimoto et al., 2011) and higher indices of insulin resistance in early and late childhood (Krishnaveni et al., 2014; Yajnik et al., 2008), albeit effect sizes are small. In one study, maternal plasma folate concentrations >16.2 nmol/L (>7.15 µg/L) and vitamin B12 levels >178 pmol/L after the first trimester were associated with increased risk of atopic dermatitis in childhood (Jong et al., 2012). Furthermore, very high levels of maternal plasma folate at delivery (≥60.3 nmol/L, 26.6 µg/L), which was apparent in 8.7% of participants in the current study, was associated with a 2.5-fold increased risk of autism spectrum disorder in the offspring (Raghavan et al., 2018).

Nonsupplement users in the current study had significantly lower plasma folate concentrations compared with MMN supplement users and these included participants with the three lowest values, ranging 3.7–5.4 µg/L. Folate deficiency is generally considered at plasma concentrations <3 µg/L (<6.8 nmol/L), at which point megaloblastic anaemia is more likely to occur (Cordero et al., 2015). For the prevention of neural tube defects in females of reproductive age, the World Health Organization has recommended a threshold for red blood cell folate concentrations only (>400 µg/L) given that plasma/serum folate concentrations have more biological variation (Cordero et al., 2015). Although we did not measure red blood cell folate concentrations in the current study, nonsupplement users are at greater risk of folate deficiency and should be counselled on appropriate dietary sources of folate, especially during the periconceptional period. There was no significant difference in plasma folate concentrations between supplement users of individual folic acid only (13.5 µg/L, $n = 8$) versus MMN supplement only (17.4 µg/L, $n = 69$), despite higher total intakes in the latter group. This suggests that MMN supplementation is not superior to individual folic acid supplementation for adequate folate status in second trimester.

In the current study, not a single participant reported taking an individual iodine supplement, despite this being the only recommended supplement at this pregnancy stage, along with other individual supplements when required (Australian Government Department of Health and Aged Care, 2020). Virtually, all MMN supplements, however, contain iodine and, as such, the majority of participants met the EAR for iodine, that is, 83.5% met the EAR for iodine but only 16.5% met the EAR from food alone. Although total iodine intake was higher among MMN users versus nonusers, there was no difference in plasma or urine iodine concentrations nor the prevalence of iodine insufficiency (indicated by urinary iodine concentration <150 µg/L). Iodine concentration in spot urine samples are frequently used for monitoring iodine status, but this reflects recent intake, has significant intra- and interday variability and may not provide a reliable estimate of habitual iodine exposure (König et al., 2011). In alignment with this, a previous study reported on adverse neurodevelopmental outcomes in children with both low and high iodine intakes, but there was no association with urinary iodine concentration (Zhou et al., 2019). Subsequent analyses identified iodine intakes <185 and >350 µg/day to be driving the association with lower neurodevelopmental scores. More than 40% of our study population had iodine intakes outside of this range, with approximately equal numbers at either end. This questions the safety of universal recommendations for iodine supplementation in pregnancy, particularly in countries with mandatory iodine fortification. An important ongoing Australian study will define the effects of reducing supplemental iodine intake during pregnancy, in people who meet the EAR from diet alone, on child cognitive development (Best et al., 2023).

The UL for iron, 45 mg/day, is based on gastrointestinal symptoms associated with high intakes, including nausea and constipation in healthy populations (National Health and Medical Research Council, 2006). This limit was surpassed by almost 50% of the study population, mainly attributed to taking a MMN supplement, with or without an individual iron supplement. This contrasts a previous Australian study reporting that only 23% exceeded the iron UL in second trimester (Livock et al., 2017). A Cochrane review reported that routine elemental iron supplementation (irrespective of dose) reduced anaemia and iron deficiency at term, but clinical benefits to maternal or infant health remain inconclusive and there is an increased risk of high haemoglobin levels (>130 g/L) during pregnancy and at term (Pena-Rosas, De-Regil, Garcia-Casal, et al., 2015), although this risk is reduced with intermittent iron supplementation (Pena-Rosas, De-Regil, Malave, et al., 2015). Haemoconcentration was more likely among those consuming ≥60 mg of elemental iron per day (Pena-Rosas, De-Regil, Garcia-Casal, et al., 2015), which may be associated with adverse pregnancy outcomes, including preterm birth, small for gestational age, low birth weight, pre-eclampsia and gestational diabetes (Wu et al., 2022; Young et al., 2019). In the current study, Elevit, which contains 60 mg of elemental iron per dose, was taken by ~40% of study participants as a once per day regimen. This is despite recommendations that, if taking an iron supplement, weekly (80–300 mg) supplementation is as effective as daily (30–60 mg) for preventing iron-deficiency anaemia and has fewer side effects. It is worth noting that recommended ULs often do not consider the bioavailability of specific nutrients or the effects of surpassing limits of several nutrients at the same time (Engle-Stone et al., 2019).

Ten percent of the study population reported having diagnosed anaemia at 28 weeks' gestation. These individuals were significantly more likely to be taking an individual iron supplement (10 of 13 with diagnosed anaemia), which aligns with recommendations for specific nutrient prescriptions when required (Australian Government Department of Health and Aged Care, 2020). The recommended daily serves of dairy/alternatives was met by only 11% of the study population and this was associated with a greater likelihood of individual supplement use (9 of 14 with dairy/alternative alignment), of which seven were taking iron. While predominantly reported in children, high calcium intakes from cow's milk is associated with iron deficiency anaemia (Ziegler, 2011), albeit we were underpowered in both anaemia incidence and dairy alignment to evaluate potential associations between these variables.

A key limitation of the current study was the single time point at which dietary and supplement intakes were assessed; however, the relative contribution of diet versus supplements to nutrient adequacy have rarely been evaluated. The current study was also not powered to perform subgroup analyses of nutrient adequacy nor to examine effects on pregnancy or birth outcomes. A goal of the wider cohort study is to capture patterns and clinical effects of supplement use across different pregnancy stages and by maternal characteristics (Borg et al., 2021). Assessment of dietary and supplement intakes constituted part of a large cohort study, which included a series of other assessments and questionnaires (Borg et al., 2021) that may have led to low survey completion rates. The small sample size is an important limitation, particularly in relation to the number of participants who agreed for research contact. This impacts generalizability of the findings, noting the participant cohort was older, more educated, had a lower BMI, were twice as likely to be receiving private obstetric care (23% vs. 12%), slightly more likely to fall under shared GP care (21% vs. 15%) and had lower rates of preterm birth (5.5% vs. ~ 8.5%) and small for gestational age (2.4% vs. ~ 8.5%) compared with the broader Australian and Queensland populations (Australian Institute of Health and Welfare, 2022a, 2022b). Although this pilot study was designed to capture a representative demographic of the Queensland population (Borg et al., 2021), it remains a challenge to recruit pregnant people with complex comorbidities who are cared for in specialist clinics.

Calculations for daily dose of supplemental nutrients assumed that supplements were taken as a full dose, as directed on the label, and this was adjusted by the reported frequency. Where no brand was recorded, a conservative dose estimate was used, which may have led to underreporting of daily supplement intake. As the mean daily dose of supplemental nutrients was used, intermittent intake has not been considered, albeit >80% of supplement users reported intake 'every day and/or night.' Finally, as few as 10 participants reported individual supplement use only and, therefore, results comparing MMN supplementation versus individual folic acid and/or iron supplementation should be interpreted with caution.

Nutritionally adequate dietary patterns consisting of a wide variety of foods is consistently recommended for positive health outcomes, beyond what can be achieved from supplementation with single nutrients (Tapsell et al., 2016). In this largely high socioeconomic population, MMN supplementation was high and not consistent with recommendations. Given the low alignment with food group recommendations (Slater et al., 2020; Wilkinson et al., 2022) and the potential risks associated with MMN supplementation (Petry et al., 2020; Raghavan et al., 2018) and exceeding nutrient ULs (Pastor-Valero et al., 2011; Pena-Rosas, De-Regil, Garcia-Casal, et al., 2015; Valera-Gran et al., 2017; Vegrim et al., 2022), the promotion of nutritionally high-quality diets should be a priority for healthcare providers and public health campaigns. An increase in vegetables and red meat/vegetarian alternatives for folate and iron are especially warranted. Supplementation with folic acid during the periconceptional period should be continued at current dosage recommendations, along with other nutrient prescriptions when indicated (Australian Government Department of Health and Aged Care, 2020). Supplementation with iodine throughout pregnancy may require consideration of dietary iodine sources to minimize risks associated with high intake. Future studies are required to determine appropriate MMN supplementation regimes in high-income countries, including subpopulations who might benefit from them.

## AUTHOR CONTRIBUTIONS

All authors are members of the QFC research collaborative and contributed to study variables that were collected, and have read and approved the final manuscript. Linda A. Gallo, Sophia L. Young, Susan de Jersey, Danielle A. J. M. Schoenaker, Danielle J. Borg, Clare E. Collins, Vicki L. Clifton, and Shelley A. Wilkinson contributed to planning of the paper, data interpretation and critical manuscript review. Sarah E. Steane undertook plasma folate measurements and extracted nutrient data from reported supplements, Jack Lockett acquired serum ferritin and haemoglobin data from clinical records, and Anthony V. Perkins oversaw ICP-MS measurements for other plasma and urine nutrients. Linda A. Gallo led the data analyses, with significant input from Sophia L. Young. Linda A. Gallo led writing of the paper, with significant inputs from Shelley A. Wilkinson, Susan de Jersey and Clare E. Collins.

## ACKNOWLEDGEMENTS

The authors wish to acknowledge the contributions of William P. Perez for statistical support provided by QCIF Facility for Advanced Bioinformatics (QFAB), The University of Queensland. Vicki L. Clifton was supported by Senior Research Fellowships from the National Health and Medical Research Council (Australia). Susan de Jersey was supported by a Metro North Health Clinician Fellowship. Open access publishing facilitated by The University of Queensland, as part of the Wiley - The University of Queensland agreement via the Council of Australian University Librarians.

## CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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**How to cite this article:** Gallo, L. A., Steane, S. E., Young, S. L., de Jersey, S., Schoenaker, D. A. J. M., Borg, D. J., Lockett, J., Collins, C. E., Perkins, A. V., Kumar, S., Clifton, V. L., & Wilkinson, S. A. (2023). Dietary supplements, guideline alignment and biochemical nutrient status in pregnancy: Findings from the Queensland Family Cohort pilot study. *Maternal & Child Nutrition*, e13589. https://doi.org/10.1111/mcn.13589