



# Determinants of folic acid supplement use outside national recommendations for pregnant women: results from the Growing Up in New Zealand cohort study

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## Abstract

**Objective:** To evaluate the sociodemographic and lifestyle factors associated with insufficient and excessive use of folic acid supplements (FAS) among pregnant women.

**Design:** A pregnancy cohort to which multinomial logistic regression models were applied to identify factors associated with duration and dose of FAS use.

**Setting:** The Growing Up in New Zealand child study, which enrolled pregnant women whose children were born in 2009–2010.

**Subjects:** Pregnant women (*n* 6822) enrolled into a nationally generalizable cohort.

**Results:** Ninety-two per cent of pregnant women were not taking FAS according to the national recommendation (4 weeks before until 12 weeks after conception), with 69% taking insufficient FAS and 57% extending FAS use past 13 weeks' gestation. The factors associated with extended use differed from those associated with insufficient use. Consistent with published literature, the relative risks of insufficient use were increased for younger women, those with less education, of non-European ethnicities, unemployed, who smoked cigarettes, whose pregnancy was unplanned or who had older children, or were living in more deprived households. In contrast, the relative risks of extended use were increased for women of higher socio-economic status or for whom this was their first pregnancy and decreased for women of Pacific *v.* European ethnicity.

**Conclusions:** In New Zealand, current use of FAS during pregnancy potentially exposes pregnant women and their unborn children to too little or too much folic acid. Further policy development is necessary to reduce current socio-economic inequities in the use of FAS.

## Keywords

Pregnancy  
Folic acid supplementation  
Public health  
Health behaviour  
Growing Up in New Zealand

Many countries have implemented folic acid supplementation (FAS) pre-pregnancy and during the first trimester of pregnancy, due to the unequivocal evidence for its protection against neural tube defects (NTD)<sup>(1,2)</sup>. However, adherence with this policy is often poor, with use of folic acid supplements (FAS) being reported for <50% of pregnant women in several countries, including Australia, Canada, the UK, the USA, Pakistan, Indonesia and China<sup>(3–6)</sup>. Factors that have been associated with inadequate use of FAS among women include younger age, belonging to particular ethnic groups, single

relationship status, multiparity, unplanned pregnancy, a less healthy lifestyle and poorer socio-economic conditions<sup>(3,7,8)</sup>.

In addition to the prevention of NTD, maternal FAS in the pre-pregnancy and/or early pregnancy period is associated with a reduced risk of other disorders, including congenital heart defects<sup>(9)</sup>, small-for-gestational-age birth<sup>(10)</sup>, language delay<sup>(11)</sup>, behavioural problems<sup>(12)</sup> and autistic spectrum disorder<sup>(13–16)</sup>. However, emerging evidence suggests a U-shaped relationship of maternal folate status during pregnancy with birth and childhood health

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outcomes. Studies have reported associations of increased exposure to folic acid (in duration and/or dose) with an increased risk of several adverse health outcomes<sup>(17,18)</sup>, including large-for-gestational-age birth<sup>(19)</sup>, insulin resistance<sup>(20–22)</sup>, increased adiposity<sup>(21)</sup>, lower psychomotor scores<sup>(23)</sup> and asthma<sup>(24)</sup>.

It is now recognized that there is the need to identify groups within populations at increased risk of both insufficient and excessive periconceptional FAS use<sup>(17)</sup>. The opportunity to determine the prevalence of both insufficient and excessive use of FAS and the factors associated with each in New Zealand (NZ) was created by the establishment of a large cohort study into which enrolment occurred during the last trimester of pregnancy. We have previously used the data collected in this cohort study to show that only 39% of women reported starting FAS before pregnancy<sup>(8)</sup>. To date though, there has been no investigation describing the adherence to the NZ Ministry of Health (MoH) recommendations for FAS during pregnancy that considers both insufficient and excessive use.

Our aim was to describe the use of FAS during pregnancy and to identify the sociodemographic and lifestyle factors associated with insufficient and excessive use of FAS in a nationally generalizable birth cohort study<sup>(25)</sup>.

## Methods

### *The Growing Up in New Zealand study*

Growing Up in New Zealand (GUiNZ) is a multi-ethnic nationally representative longitudinal birth cohort study, consisting of 6853 children born to 6822 women enrolled while pregnant<sup>(25,26)</sup>. As described previously, pregnant women were eligible if they had an estimated delivery date between 25 April 2009 and 25 March 2010 and were living in a geographical region defined by the three contiguous District Health Boards of Auckland, Counties-Manukau and Waikato<sup>(26)</sup>. For the present study, we utilized data from the first collection wave (antenatal period; completed in 2010). Data were collected at a face-to-face home computer-assisted personal interview conducted with each pregnant woman, most often in the last trimester of her pregnancy. Linkage was established to perinatal health records, providing information about the latter stages of pregnancy, the birth and the immediate neonatal period.

### *Assessment of folic acid supplement use*

#### *Subsidized folic acid supplements dispensed from community pharmacies*

Folic acid tablets are available over the counter from pharmacies in NZ and are also dispensed, at a lower cost, to pregnant women with a prescription. All the prescribed dispensing from community pharmacies is recorded in the NZ MoH Pharmaceutical Collection database<sup>(27)</sup>. Data linkage with the Pharmaceutical Collection database

identified FAS dispensed by pharmacists to the women participating in the GUiNZ cohort study from when their pregnancy was confirmed (mostly in the first trimester of pregnancy). The GUiNZ study obtained consent to access women's pharmaceutical information only for their pregnancy with the cohort child. For this reason, the data on pharmacy dispensing in the pre-pregnancy period were not available for use in the present study. FAS dispensed from pharmacies were described according to the tablets' folic acid content (folic acid 5 mg, folic acid 0.8 mg, folic acid 0.35 mg with a ferrous compound).

Using the infant's gestational age at birth we estimated the gestational age of each woman when first dispensed FAS and simulated the total number of weeks of FAS using the pharmacy dispensing date and number of tablets dispensed (assuming the use of 1 tablet/d). Information on use, duration of use and dose of FAS was available for 6044/6822 (89%) of the women. After additional exclusions from missing Pharmaceutical Collection data, the final sample was 5857/6822 (86%) women.

#### *Maternal report of folic acid supplement use*

The use of FAS was evaluated in three time periods: 3 months before pregnancy, during the first trimester of pregnancy and after the first trimester of pregnancy. For each of those time intervals the following questions were asked: 'Have you taken folate or folic acid, even as part of a multivitamin?', 'How many days per week on average?' and 'For how many weeks?'

The current NZ MoH policy on use of FAS for reducing NTD in NZ is the same as that in place at the time of the present study. In NZ it is recommended that women at low risk of an NTD-affected pregnancy and who plan to become pregnant take 0.8 mg of folic acid daily for 4 weeks before until 12 weeks after conception<sup>(28)</sup>. For women at high risk of an NTD-affected pregnancy the recommendation is to take a higher dosage (5 mg of folic acid daily) during the same time period. The NZ MoH considers women at high risk as those: with a previous NTD-affected pregnancy; or with a close family member who has had an NTD; or who are on insulin for diabetes, or who are taking medications known to affect folate metabolism; or whose partner is affected or has a family history of NTD<sup>(28)</sup>.

Based on the reported FAS, the study population was divided in five categories. The category 'no use' refers to the women who did not use FAS either before or during the pregnancy. The category 'recommended use' refers to women who used FAS 6–7 times/week in at least 4 weeks pre-pregnancy and for 12 weeks after conception. The category 'recommended and extended use' refers to the women who used FAS according to recommendation but then also extended its use after the first trimester. The category 'insufficient use' refers to the women who did not take FAS as recommended in early pregnancy. The category 'insufficient and extended use' refers to the women

who did not take enough FAS in early pregnancy but extended its use after the first trimester of pregnancy.

**Assessment of covariates**

Variables describing maternal self-prioritized ethnicity, age, education, relationship status, employment, parity, alcohol consumption, smoking patterns, pregnancy planning, and sources of information about vitamins and minerals were collected during the antenatal interview.

Maternal self-prioritized ethnicities were self-reported. Response options provided a list of thirty-three ethnicities, with the ability for participants to indicate alternative 'other' ethnicities in addition to those listed. Ethnicity was then coded into six Level 1 categories following the Statistics NZ coding criteria: (i) European, (ii) Māori, (iii) Pacific Peoples, (iv) Asian, (v) Middle Eastern, Latin American and African (MELAA) and (vi) other, with MELAA and other then combined for analysis purposes because of the smaller sizes of these two groups.

Socio-economic deprivation was described using the 2006 NZ Index of Deprivation (NZDep06), grouped as deciles. NZDep06, derived from 2006 census data on nine socio-economic characteristics, is a well-validated measure of small area socio-economic deprivation in NZ<sup>(29)</sup>.

Maternal self-reported weight (in kilograms) and height (in centimetres) during pregnancy were collected and BMI calculated and categorized according to WHO criteria<sup>(30)</sup>. During pregnancy, self-reported height and weight have been shown to classify the majority (84%) of women into appropriate BMI categories<sup>(31)</sup>.

**Statistical analyses**

Proportions, means, medians and interquartile ranges were used to describe the population and the FAS use. Proportions were compared with the  $\chi^2$  test. Associations between the categories of FAS use and maternal socio-demographic and lifestyle characteristics were described using relative risk ratios (RRR) and 95% CI obtained from multivariate multinomial logistic regression models. The women who used FAS during pregnancy as recommended formed the reference group for these analyses. Participants with missing values for any of the covariates were excluded from the final multivariate model.

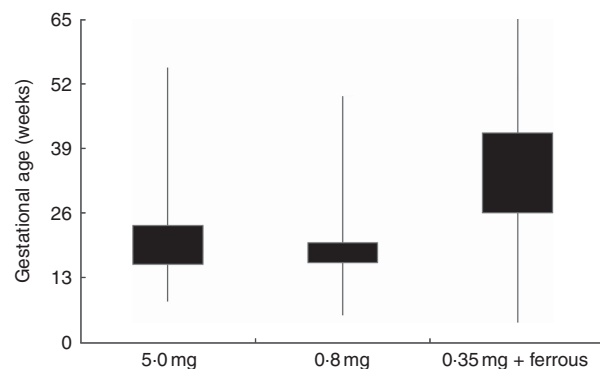
All analyses were performed using the Stata statistical software package release 12 (2011). Two-sided significance was determined at  $P < 0.05$ .

**Results**

**Folic acid dispensed from pharmacies to cohort women**

For 29.6% (1791/6044) of the women, FAS were reported to have been used during the pregnancy and were also dispensed from a pharmacy. Additionally, 3.1% (188/6044) of the women were dispensed folic acid tablets but did not report using FAS. Overall, a mean of eighty-nine tablets containing folic acid were dispensed per woman. Of the tablets dispensed, 71% contained 0.8 mg of folic acid, 15% contained 5 mg of folic acid and 14% contained 0.35 mg with a ferrous compound (Table 1).

Figure 1 illustrates the distribution of gestational age of the women during the time they were dispensed folic acid tablets. More than 75% of the women who were dispensed folic acid tablets, in its different formulations,



**Fig. 1** Box-and whisker plot showing the potential duration\* of use of subsidized folic acid supplements according to the type of tablet dispensed in New Zealand, 2008–2010. The bottom and top edge of the boxes represent the 25th and 75th percentile (interquartile range), respectively; and the ends of the bottom and top whiskers represent the minimum and maximum values, respectively, of gestational age in weeks. \*Potential duration of use of subsidized tablets was estimated using infant's gestational age at birth, gestational age when the woman was first dispensed folic acid tablets and the number of tablets dispensed (assuming the use of 1 tablet/d)

**Table 1** Number and proportion of women according to category of folic acid supplement use, pharmacy dispensing and type of supplement dispensed in New Zealand, 2008–2010

Pharmacy dispensing and type of supplement	'None'		'Insufficient'		'Insufficient and extended'		'Recommended'		'Recommended and extended'		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Not dispensed	781	80.6	674	51.3	1219	62.6	307	69.1	1084	79.0	4065	67.3
Dispensed	188	19.4	639	48.7	727	37.4	137	30.9	288	21.0	1979	32.7
5 mg	24	12.1	86	12.8	122	15.4	17	11.9	56	18.6	305	14.5
0.8 mg	128	64.7	528	78.7	539	68.1	104	72.7	197	65.2	1496	71.1
0.35 mg + ferrous	46	23.2	57	8.5	130	16.4	22	15.4	49	16.2	304	14.4

potentially extended its use beyond the first trimester of pregnancy.

### Maternal report of folic acid supplement use

Only a small proportion of women (7.6%) reported the use of FAS as recommended, with another 23.4% reporting using FAS according to the recommendation but with extension into the second trimester of pregnancy. Thirteen per cent of the women reported no use of FAS either before or during pregnancy. Almost one-quarter of the women (22.4%) had insufficient use of FAS in early pregnancy and 33.3% had insufficient use of FAS in early pregnancy but extended its use beyond the first trimester.

The majority of women in the 'insufficient and extended' use group did not use FAS during the pre-pregnancy period but used 6–7 folic acid tablets/week from the first trimester of pregnancy. Ninety-two per cent of the women in the 'recommended and extended use' group continued using 6–7 folic acid tablets/week after the first trimester of pregnancy, for a median of an additional 20 weeks (interquartile range = 15–26 weeks; Table 2).

### Maternal sociodemographic and lifestyle characteristics

Over one-half (55.2%) of the women identified themselves as European, 30.6% had completed at least a diploma/trade certificate, for 61.3% the current pregnancy was planned and 37.2% lived in the most deprived households. Higher level of education, more social support (relationship status), employment, having a planned pregnancy and living in a less deprived household were more prevalent when FAS was used according to the

recommendation, as identified by the 'recommended use' and 'recommended and extended use' categories when compared with the 'no use', 'insufficient use' and 'insufficient and extended use' (Table 3).

### Determinants of folic acid supplement use

In the univariate analyses, all the variables describing women's sociodemographic and lifestyle characteristics were associated with the categories of FAS use (see online supplementary material, Supplemental Table 1).

The results of the multivariate analysis with the independent associations of maternal characteristics with the categories of FAS use are presented in Table 4. The variables nutritional status, relationship status and alcohol consumption before pregnancy were excluded from the multivariate analyses because they were not associated with any category of FAS use. In the multivariate analysis, the two factors independently associated with all FAS categories of use, when compared with the 'recommended' group, were self-prioritized ethnicity and parity. Pregnancy planning, education and age were independently associated with the 'none', 'insufficient use' or 'insufficient and extended use' groups. Smoking was independently associated with the 'none' or 'insufficient use' group. Work status and household deprivation were factors independently associated with the 'none' group (Table 4).

### Sources of information about vitamins and minerals during pregnancy

The main sources of information about vitamins and minerals during pregnancy were health-care professionals (83.3%), family and friends (31.4%) and media (31.3%; Table 5).

**Table 2** Distribution of women by category of folic acid supplement (FAS) use, reported dose of FAS used per week and reported duration of FAS use (weeks) in the pre-pregnancy period, first trimester and after the first trimester of pregnancy in New Zealand, 2008–2010

Period and average dose of FAS use per week	None		'Insufficient'		'Insufficient and extended'				'Recommended'				'Recommended and extended'					
	n	%	n	%	Duration*		n	%	Duration*		n	%	Duration*		n	%	Duration*	
					Median	IQR			Median	IQR			Median	IQR			Median	IQR
<b>Pre-pregnancy</b>																		
0 tablets/week	781	100.0	1101	84.0	–	–	1621	83.3	–	–	0	0.0	–	–	0	0.0	–	–
1–2 tablets/week	0	0.0	29	2.2	4	3–11	59	3.0	6	4–13	0	0.0	–	–	0	0.0	–	–
3–5 tablets/week	0	0.0	70	5.3	10	6–13	149	7.6	12	8–13	0	0.0	–	–	0	0.0	–	–
6–7 tablets/week	0	0.0	113	8.6	6	3–12	118	6.1	4	2–12	444	100.0	12	8–13	1372	100	13	12–13
<b>First trimester</b>																		
0 tablets/week	781	100.0	47	3.6	–	–	234	12.0	–	–	0	0.0	–	–	0	0.0	–	–
1–2 tablets/week	0	0.0	59	4.5	10	4–12	53	2.7	12	7–13	0	0.0	–	–	0	0.0	–	–
3–5 tablets/week	0	0.0	133	10.1	10	4–12	171	8.8	12	7–13	0	0.0	–	–	0	0.0	–	–
6–7 tablets/week	0	0.0	1074	81.8	12	7–12	1489	76.5	12	7–13	444	100.0	12	12–13	1372	100	13	12–13
<b>After first trimester</b>																		
0 tablets/week	781	100.0	1313	100.0	–	–	0	0.0	–	–	0	0.0	–	–	0	0.0	–	–
1–2 tablets/week	0	0.0	0	0.0	–	–	139	7.1	13	5–22	0	0.0	–	–	34	2.5	14	8–21
3–5 tablets/week	0	0.0	0	0.0	–	–	237	12.2	16	8–26	0	0.0	–	–	82	6.0	16	12–26
6–7 tablets/week	0	0.0	0	0.0	–	–	1571	80.7	17	10–26	0	0.0	–	–	1256	91.5	20	15–26

IQR, interquartile range.

\*Duration in weeks.

**Table 3** Sociodemographic and lifestyle characteristics of women according to the category of folic acid supplement use in New Zealand, 2008–2010

Characteristic	'None'		'Insufficient'		'Insufficient and extended'		'Recommended'		'Recommended and extended'		Total		P*
	n	%	n	%	n	%	n	%	n	%	n	%	
Total	781	13.3	1313	22.4	1947	33.2	444	7.6	1372	23.4	5857	100	
Age (years)													<0.001
≤29	503	64.4	735	56.0	900	46.2	102	23.0	302	22.0	2542	43.4	
>29	278	35.6	578	44.0	1047	53.8	342	77.0	1070	78.0	3315	56.6	
Level of education													<0.001
Higher degree	17	2.2	148	11.3	287	14.8	125	28.2	393	28.6	970	16.6	
Bachelor's degree	56	7.2	240	18.3	497	25.6	129	29.0	433	31.6	1355	23.2	
Diploma/trade certificate	261	33.6	474	36.2	613	31.5	110	24.8	330	24.1	1788	30.6	
≤Secondary school/NCEA 1–4	443	57.0	447	34.2	547	28.1	80	18.0	216	15.7	1733	29.6	
Self-prioritized ethnicity													<0.001
European	118	15.1	620	47.3	1070	55.1	348	78.4	1074	78.3	3230	55.2	
Māori	234	30.0	238	18.2	234	12.1	20	4.5	64	4.7	790	13.5	
Pacific	349	44.7	221	16.9	174	9.0	18	4.1	16	1.2	778	13.3	
Asian	66	8.5	176	13.4	391	20.1	43	9.7	162	11.8	838	14.3	
Other†	13	1.7	55	4.2	73	3.8	15	3.4	55	4.0	211	3.6	
BMI‡ (kg/m <sup>2</sup> )													<0.001
≤24.9	193	35.9	627	54.9	1087	61.9	284	67.0	882	66.3	3073	59.2	
25.0–29.9	135	25.1	286	25.1	368	21.0	81	19.1	300	22.6	1170	22.6	
≥30.0	210	39.0	228	20.0	300	17.1	59	13.9	148	11.1	945	18.2	
Relationship status													<0.001
No relationship	180	23.2	138	10.5	188	9.7	11	2.5	18	1.3	535	9.2	
Cohabiting	269	34.6	464	35.5	573	29.5	83	18.7	238	17.4	1627	27.8	
Married or civil union	328	42.2	707	54.0	1183	60.9	350	78.8	1114	81.3	3682	63.0	
Work													<0.001
Employed	218	27.9	635	48.4	1104	56.7	296	66.7	960	70.0	3213	54.9	
Unemployed	136	17.4	142	10.8	155	8.0	15	3.4	55	4.0	503	8.6	
Student	64	8.2	102	7.8	153	7.9	34	7.7	88	6.4	441	7.5	
Not in workforce	363	46.5	434	33.1	535	27.5	99	22.3	269	19.6	1700	29.0	
Parity													<0.001
First born	197	25.2	520	39.6	885	45.5	191	43.0	681	49.6	2474	42.2	
Subsequent	584	74.8	793	60.4	1062	54.6	253	57.0	691	50.4	3383	57.8	
Pregnancy planned													<0.001
Yes	221	28.3	663	50.5	1008	51.8	415	93.5	1283	93.5	3590	61.3	
No	560	71.7	650	49.5	939	48.2	29	6.5	89	6.5	2267	38.7	
Alcohol before pregnancy (per week)													<0.001
Did not drink	310	39.8	389	29.7	553	28.4	96	21.7	288	21.0	1636	28.0	
≤3 drinks	234	30.0	528	40.3	820	42.1	221	49.9	707	51.5	2510	42.9	
>3 drinks	235	30.2	394	30.0	574	29.5	126	28.4	377	27.5	1706	29.1	
Pre/during pregnancy smoking pattern													<0.001
Non-smoker	453	58.1	947	72.5	1578	81.3	416	93.7	1286	94.0	4680	80.1	
Continued/stopped smoking	327	41.9	360	27.5	364	18.7	28	6.3	82	6.0	1161	19.9	
Household deprivation§													<0.001
1 to 3	42	5.4	279	21.2	503	25.9	158	35.6	516	37.6	1498	25.6	
4 to 7	154	19.7	442	33.7	792	44.0	185	41.7	604	44.0	2177	37.2	
8 to 10	585	74.9	592	45.1	252	18.4	101	22.7	252	18.4	2180	37.2	

NCEA, National Certificate of Educational Achievement.

\*The  $\chi^2$  test was used to determine if any significant differences existed among the groups according to maternal characteristics ( $P < 0.05$  indicates there is difference).

†Others include Middle Eastern, Latin American, African and others.

‡BMI: underweight and eutrophic,  $\leq 24.9$  kg/m<sup>2</sup>; overweight, 25.0–29.9 kg/m<sup>2</sup>; and obese,  $\geq 30.0$  kg/m<sup>2</sup>.

§Area-level socio-economic deprivation was measured using the NZ Index of Deprivation: decile 1, 2 and 3 = least deprived households; decile 8, 9 and 10 = most deprived households.

**Table 4** Adjusted relative risk ratios (RRR) and 95% CI for the association of maternal sociodemographic and lifestyle characteristics with category of folic acid supplement use in New Zealand, 2008–2010

Characteristic*	'None'		'Insufficient'		'Insufficient and extended'		'Recommended and extended'	
	RRR	95% CI	RRR	95% CI	RRR	95% CI	RRR	95% CI
Age (years)								
≤29	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
>29	0.38	0.28, 0.52	0.39	0.29, 0.51	0.54	0.42, 0.70	1.09	0.83, 1.43
Level of education								
Higher degree	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Bachelor's degree	2.11	1.12, 3.94	1.17	0.84, 1.63	1.31	0.97, 1.76	1.08	0.82, 1.44
Diploma/trade certificate	3.66	2.02, 6.63	1.54	1.10, 2.16	1.39	1.02, 1.91	1.03	0.76, 1.40
≤Secondary school/NCEA 1–4	4.92	2.68, 9.06	1.44	0.99, 2.08	1.40	0.99, 1.98	0.96	0.68, 1.36
Self-prioritized ethnicity								
European	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Māori	7.09	4.13, 12.16	2.54	1.53, 4.2	1.76	1.07, 2.89	1.13	0.66, 1.91
Pacific	14.36	8.17, 25.24	3.12	1.82, 5.32	1.79	1.05, 3.05	0.33	0.16, 0.67
Asian	4.56	2.85, 7.28	2.15	1.47, 3.13	2.67	1.87, 3.80	1.23	0.85, 1.78
Others†	2.04	0.90, 4.59	1.88	1.02, 3.45	1.50	0.83, 2.69	1.21	0.67, 2.18
Work								
Employed	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Unemployed	2.01	1.09, 3.71	1.44	0.80, 2.57	1.23	0.69, 2.19	1.25	0.69, 2.28
Student	1.41	0.85, 2.35	0.92	0.60, 1.43	0.93	0.61, 1.41	0.83	0.54, 1.26
Not in workforce	1.74	1.25, 2.42	1.14	0.86, 1.51	0.98	0.74, 1.28	0.92	0.70, 1.21
Parity								
First born	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Subsequent	2.80	2.07, 3.78	1.48	1.16, 1.90	1.12	0.89, 1.41	0.78	0.62, 0.98
Pregnancy planned								
Yes	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
No	13.12	8.54, 20.14	8.12	5.43, 12.13	9.86	6.64, 14.63	1.05	0.67, 1.63
Pre/during pregnancy smoking pattern								
Non-smoker	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Continued/stopped smoking	2.86	1.82, 4.49	2.35	1.53, 3.62	1.77	1.16, 2.71	1.01	0.64, 1.59
Household deprivation‡								
1 to 3	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
4 to 7	1.68	1.09, 2.60	0.97	0.74, 1.28	1.03	0.80, 1.33	0.99	0.77, 1.26
8 to 10	2.98	1.90, 4.68	1.19	0.87, 1.65	0.99	0.73, 1.34	0.80	0.59, 1.09

NCEA, National Certificate of Educational Achievement; Ref., reference category.

\*Multivariate multinomial logistic regression models included all variables presented in the table. The group of women who reached the recommendation for folic acid use was the reference in this analysis (two-sided significance was determined at  $P < 0.05$ ).

†Others include Middle Eastern, Latin American, African, and others.

‡Area-level socio-economic deprivation was measured using the NZ Index of Deprivation: decile 1, 2 and 3=least deprived households; decile 8, 9 and 10=most deprived households.

**Table 5** Number and proportion of women, according to category of use of folic acid supplements, using different sources of information about vitamins and minerals during pregnancy in New Zealand, 2008–2010

Source of information about vitamins and minerals	'None'		'Insufficient'		'Insufficient and extended'		'Recommended'		'Recommended and extended'		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Health-care professionals	358	92.3	1149	88.1	1589	82.1	372	84.4	1059	77.5	4527	83.3
Midwife	278	71.7	763	58.5	1114	57.5	222	50.3	615	45.0	2992	55.0
General practitioner (family doctor)	139	35.8	668	51.2	879	45.4	237	53.7	569	41.7	2492	45.8
Others†	11	2.8	150	11.5	286	14.8	88	20.0	404	29.6	939	17.3
Family and friends	60	15.5	316	24.2	679	35.1	129	29.3	524	38.4	1708	31.4
Friends	25	6.4	185	14.2	431	22.3	85	19.3	353	25.8	1079	19.9
Family	49	12.6	206	15.8	427	22.1	74	16.8	301	22.0	1057	19.4
Media	40	10.3	276	21.2	658	34.0	143	32.4	584	42.8	1701	31.3
Books, magazines, newspaper	20	5.2	151	11.6	316	16.3	86	19.5	315	23.1	888	16.3
Television	12	3.1	102	7.8	277	14.3	37	8.4	219	16.0	647	11.9
Others‡	17	4.4	108	8.3	262	13.5	61	13.8	250	18.3	698	12.8

†Other health-care professionals include obstetrician, alternative health practitioner and dietitian/nutritionist.

‡Other media sources include Internet, pharmacy/retailer and radio.

## Discussion

Ninety-two per cent of pregnant women from this nationally generalizable birth cohort study in NZ were not taking FAS as recommended. Thirteen per cent of pregnant women did not use FAS at any time, with non-use

associated with age, education, ethnicity, employment, parity, pregnancy planning, smoking and household deprivation. One-quarter of the women had insufficient use of FAS during pregnancy and this insufficient use was associated with age, education, ethnicity, parity, pregnancy planning and smoking. One-third of the women



had insufficient use of FAS in early pregnancy and then extended its use beyond the first trimester. This pattern of FAS use was associated with age, education, ethnicity, parity and pregnancy planning. The remaining quarter of women initially achieved the recommendation but then extended FAS use beyond the first trimester of pregnancy, and this pattern was associated with ethnicity and parity. Health-care professionals were the main sources of information about vitamins and minerals, followed by family and friends. For only 35% of the pregnant women was FAS use during pregnancy both self-reported and confirmed by receipt of subsidized folic acid tablets dispensed from a pharmacy.

Improving adherence of pregnant women with national recommendations for FAS is a challenge faced by many countries. In most European countries, a minority of women take FAS during the entire period recommended (4 weeks before conception until 8 weeks after), ranging from 3% in Italy to 51% in the Netherlands (where 85% of pregnancies are believed to be planned)<sup>(32,33)</sup>. In Australia, from 28 to 46% of women use FAS periconceptionally<sup>(7)</sup>. Approximately 39% of NZ women in the GUiNZ cohort started using FAS before pregnancy<sup>(8)</sup>, but only 8% used it as recommended both pre- and post-conception. Lack of pregnancy planning is likely to be one of the main reasons for the proportion of women who used FAS as directed being as low as it was in our cohort. We have previously shown that the odds of starting FAS prior to the pregnancy were approximately ten times lower for women whose pregnancy was not planned compared with women whose pregnancy was planned<sup>(8)</sup>. Another potential reason for the high prevalence of non-use of FAS within the GUiNZ cohort could be the lack of adequate and complete information about the importance of taking FAS during pregnancy. While almost all women in the cohort had engaged with a lead maternity carer for their antenatal care (98%), for 8 to 14% of them engagement with a lead maternity carer was delayed past 10 weeks of gestation<sup>(34)</sup>.

The determinants of inadequate FAS use during pregnancy have been reported in other studies<sup>(3-7,35)</sup>. Those women who are younger, from lower incomes and educational levels, with less social support, or of a minority ethnic group are less likely to take FAS<sup>(7,36)</sup>. These associations were also evident in our study and highlight that the current policy provides the poorest protection against NTD for women who have the least resources available to care for a child with an NTD<sup>(37)</sup>.

In contemporary society where information is available from many sources and where folic acid is easily accessed (via supplements and fortified food), excessive intake becomes a potentially important issue<sup>(18)</sup>. Despite the limited number of published data on the prevalence of FAS use which exceeds recommendations, recent studies have suggested that excessive maternal folic acid can influence fetal programming, with this being of relevance to the subsequent development of diabetes<sup>(20-22)</sup>,

asthma<sup>(24)</sup>, and neurological and psychiatric diseases<sup>(13,23,38)</sup>. In an Indian cohort of 533 pregnant women and their children, higher maternal folate concentrations (plasma level assessed at 30 weeks' gestation) were associated with higher homeostatic model assessment of insulin resistance in the children at 9.5 and 13.5 years of age<sup>(21)</sup>. The Generation 1 cohort study of Australian families (*n* 557), where mothers reported retrospectively about consumption of FAS, showed that FAS in late pregnancy (30-34 weeks) was associated with an increased odds of asthma when the cohort children were 3.5 years of age<sup>(24)</sup>. In the same study, 16% of women used FAS in pre-pregnancy, early and late pregnancy and 12% used in early and late pregnancy, compared with 23% ('recommended and extended use') and 33% ('insufficient and extended use'), respectively, in the GUiNZ study<sup>(24)</sup>. A population-based cohort study in a Chinese province found that among those who took FAS in the first trimester, 18% extended supplement use for the second and/or third trimester of pregnancy<sup>(19)</sup>.

The prevalence of extended use of FAS in NZ is high and it will be important to determine if such use is associated with any adverse health outcomes, for example increased adiposity, insulin resistance and asthma. Two distinct groups of extended use were apparent. In common, a larger proportion of both groups reported accessing information about vitamin and mineral use during pregnancy from family, friends and television than did women in other categories of FAS use. The women in the 'recommended and extended use' group were comparable to those in the 'recommended use group'. They were older, had better sociodemographic indicators and, for a larger proportion of them, the pregnancy was planned. Other studies have reported similar demographic characteristics among those with extended use of folic acid<sup>(19)</sup>. In comparison with the 'recommended use' group, for a larger proportion of those in the 'recommended and extended use' group this was their first pregnancy. During the first pregnancy fears for the well-being of the fetus are increased, enhancing the perception of risk to their baby that could potentially make extended use of folic acid more likely to occur<sup>(39,40)</sup>.

In NZ, there is no pre-approval process by the NZ Medicines and Medical Devices Safety Authority for dietary supplements to be sold and the sponsor is responsible to ensure the product is safe and complies with the Dietary Supplements Regulations 1985<sup>(41)</sup>. Between 2008 and 2010, there were thirty-three different dietary supplements available in NZ that contained folic acid, seventeen of which were sold in pharmacies only<sup>(42)</sup>. More than 60% of pregnant women who reported using FAS in the GUiNZ study had not been dispensed subsidized tablets, which implies they were buying these supplements from pharmacies or other retail stores. Yet, within the subsidized dispensation system, there should be a mechanism to control FAS use and to prevent the potential for extended



use of this supplement (Fig. 1). We hypothesize that the potential for extended use arises because of the lack of precise calculation of the number of tablets dispensed and that prescriptions remain valid for 3 months after the date they are written. Thus, health-care professionals' prescribing appears to contribute to at least some of this extended FAS use<sup>(43)</sup>.

Subsidized folic acid tablets with dosages of 0.8 mg and 5 mg are the only registered folic acid preparations available over the counter from pharmacies in NZ<sup>(28)</sup>. The NZ policy recommends a dosage of folic acid for women at low risk of an NTD-affected pregnancy that is twice as high as that recommended by the WHO and adopted by several countries<sup>(2)</sup>. To avoid or minimize its excessive use, the available dose of folic acid in supplements and multivitamins in NZ could be reduced to 0.4 mg/d for women at low risk of an NTD-affected pregnancy<sup>(44)</sup>.

Among the GUiNZ participants who were dispensed subsidized FAS from pharmacies, 15% (*n* 305) took tablets containing 5 mg of folic acid. The frequency of this higher-dose prescription seems higher than the prevalence of women with increased risk of NTD (family history of NTD, use of medications known to affect folate metabolism and/or insulin treatment for diabetes)<sup>(28)</sup>. For example, the self-reported prevalence of diabetes (before and/or during the current pregnancy) was 4.6% among those who were dispensed FAS in the GUiNZ study (data not shown). A Spanish multicentre mother and child cohort study (*n* 2226) suggested that high dose of FAS (5 mg/d) during pregnancy, used by almost 3.5% of mothers, was associated with lower psychomotor development of infants at 1 year of age<sup>(23)</sup>. These findings suggest the need for better education of health-care providers regarding folic acid prescribing practices.

Our study findings provide an important foundation upon which policy makers could develop strategies to ensure that neither insufficient nor excessive use of FAS increases the risk of poor outcomes for the mother and/or her child. Some strategies have been described to be effective interventions for improving FAS use mainly among disadvantaged women<sup>(7)</sup>. As a potential short-term intervention, the importance of FAS could be addressed during routine family doctor visits, for example during routine cervical screening with women who are less likely to use FAS. NZ is in the highest five of OECD (Organisation for Economic Co-operation and Development) countries in terms of cervical screening rates (76.7% of total coverage), although with lower coverage rates among Māori (65.5%) and Asian (64.8%) populations<sup>(7,45)</sup>. During antenatal care appointments health professionals should discuss with women, more likely to use FAS beyond the recommendation, the possible risks associated with this behaviour. As a longer-term intervention, several studies have reported that more effective and safer prevention of NTD can be achieved with fortification of food with folic acid<sup>(46,47)</sup>. Since 1996, NZ has allowed the

voluntary fortification of bread with folic acid, but the majority of breads remain unfortified with folic acid<sup>(48)</sup>. In 2009, legislation for the mandatory fortification of wheat flour or bread with folic acid was introduced in Australia and with the intention that it would also be introduced in NZ, where the government instead decided to encourage increased voluntary fortification by the baking industry. That this legislation in Australia was effective in reducing the incidence of NTD-affected pregnancies and safe was confirmed in a 2016 report by the Australian Government<sup>(49,50)</sup>. NZ does need to reconsider the decision not to mandate for folic acid fortification. The folate status of women of childbearing age in NZ was assessed in a population-based health survey conducted in 2014–2015<sup>(51)</sup>. Sixteen per cent of the women aged 15–49 years who were included in the survey had erythrocyte folate levels accepted internationally to confer minimal risk of an NTD-affected pregnancy<sup>(51)</sup>. These data add additional support to the implementation of the fortification programme.

Our study has a number of potential limitations. The data on FAS use could be biased since this was reported retrospectively by women, most often in the last trimester of pregnancy. Such data collection methods tend to result in an overestimation of FAS use due to the social desirability of particular responses to such questions<sup>(52)</sup>. As part of the baseline and monitoring assessment, only updated national nutrition surveys, ideally with assessment of erythrocyte folate levels<sup>(53)</sup>, will allow for estimation of the prevalence of inadequate and excess folic acid intake across life-cycle groups<sup>(54–59)</sup>. We have conducted a cross-sectional analysis within the GUiNZ cohort and longitudinal analyses, with cohort sizes larger than ours, are needed in this field. A major strength of the present study is the size of the cohort, its diversity and generalizability to the current population of NZ births<sup>(25,26)</sup>. We add important findings to this field of research, given that we were able to characterize in detail the use of FAS throughout pregnancy in a nationally generalizable sample. In addition, the use of data linkage to Pharmaceutical Collection database permitted more accurate evaluation of the use of FAS<sup>(27)</sup>.

## Conclusions

A very large proportion of NZ pregnant women were not taking FAS according to the MoH recommendation, with most of them extending its use beyond the recommended duration. In NZ, the public health messaging and education on FAS during pregnancy needs to be addressed since the current strategy appears to be inadequate, creates inequity and has a potential for harm to be caused by its inappropriate implementation. The case for revising the public policy for the prevention of NTD by folic acid fortification of foods needs to be raised again in NZ. This appears to be the only policy option that would ensure greater coverage to those at risk of insufficient intake.





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## Supplementary material

To view supplementary material for this article, please visit <https://doi.org/10.1017/S1368980018000836>

## References

1. MRC Vitamin Study Research Group (1991) Prevention of neural tube defects: results of the Medical Research Council Vitamin Study. *Lancet* **338**, 131–137.
2. Gomes S, Lopes C & Pinto E (2016) Folate and folic acid in the periconceptional period: recommendations from official health organizations in thirty-six countries worldwide and WHO. *Public Health Nutr* **19**, 176–189.
3. Ray JG, Singh G & Burrows RF (2004) Evidence for sub-optimal use of periconceptional folic acid supplements globally. *BJOG* **111**, 399–408.

4. Gebreamlak B, Dadi AF & Atnafu A (2017) High adherence to iron/folic acid supplementation during pregnancy time among antenatal and postnatal care attendant mothers in governmental health centers in Akaki Kality Sub City, Addis Ababa, Ethiopia: hierarchical negative binomial Poisson regression. *PLoS One* **12**, e0169415.
5. Nisar Y Bin, Dibley MJ & Mir AM (2014) Factors associated with non-use of antenatal iron and folic acid supplements among Pakistani women: a cross sectional household survey. *BMC Pregnancy Childbirth* **14**, 305.
6. Titaley CR & Dibley MJ (2015) Factors associated with not using antenatal iron/folic acid supplements in Indonesia: the 2002/2003 and 2007 Indonesia Demographic and Health Survey. *Asia Pac J Clin Nutr* **24**, 162–176.
7. Stockley L & Lund V (2008) Use of folic acid supplements, particularly by low-income and young women: a series of systematic reviews to inform public health policy in the UK. *Public Health Nutr* **11**, 807–821.
8. Morton SMB, Grant CC & Carr PEA (2013) Too many left at risk by current folic acid supplementation use: evidence from Growing Up in New Zealand. *Aust N Z J Public Health* **37**, 190–191.
9. Feng Y, Wang S, Chen R *et al.* (2015) Maternal folic acid supplementation and the risk of congenital heart defects in offspring: a meta-analysis of epidemiological observational studies. *Sci Rep* **5**, 8506.
10. Hodgetts VA, Morris RK, Francis A *et al.* (2015) Effectiveness of folic acid supplementation in pregnancy on reducing the risk of small-for-gestational age neonates: a population study, systematic review and meta-analysis. *BJOG* **122**, 478–490.
11. Roth C, Magnus P, Schjølberg S *et al.* (2011) Folic acid supplements in pregnancy and severe language delay in children. *JAMA* **306**, 1566–1573.
12. Roza SJ, van Batenburg-Eddes T, Steegers EAP *et al.* (2010) Maternal folic acid supplement use in early pregnancy and child behavioural problems: the Generation R study. *Br J Nutr* **103**, 445–452.
13. Barua S, Kuizon S, Brown WT *et al.* (2016) DNA methylation profiling at single-base resolution reveals gestational folic acid supplementation influences the epigenome of mouse offspring cerebellum. *Front Neurosci* **10**, 168.
14. Gao Y, Sheng C, Xie R-H *et al.* (2016) New perspective on impact of folic acid supplementation during pregnancy on neurodevelopment/autism in the offspring children – a systematic review. *PLoS One* **11**, e0165626.
15. Schmidt RJ, Tancredi DJ, Ozonoff S *et al.* (2012) Maternal periconceptional folic acid intake and risk of autism spectrum disorders and developmental delay in the CHARGE (Childhood Autism Risks from Genetics and Environment) case-control study. *Am J Clin Nutr* **96**, 80–89.
16. Surén P, Roth C, Bresnahan M *et al.* (2013) Association between maternal use of folic acid supplements and risk of autism spectrum disorders in children. *JAMA* **309**, 570.
17. Choi J, Yates Z, Veysey M *et al.* (2014) Contemporary issues surrounding folic acid fortification initiatives. *Prev Nutr Food Sci* **19**, 247–260.
18. Patel KR & Sobczyńska-Malefora A (2017) The adverse effects of an excessive folic acid intake. *Eur J Clin Nutr* **71**, 159–163.
19. Wang S, Ge X, Zhu B *et al.* (2016) Maternal continuing folic acid supplementation after the first trimester of pregnancy increased the risk of large-for-gestational-age birth: a population-based birth cohort study. *Nutrients* **8**, E493.
20. Keating E, Correia-Branco A, Araujo JR *et al.* (2015) Excess perigestational folic acid exposure induces metabolic dysfunction in post-natal life. *J Endocrinol* **224**, 245–259.
21. Krishnaveni GV, Veena SR, Karat SC *et al.* (2014) Association between maternal folate concentrations during pregnancy and insulin resistance in Indian children. *Diabetologia* **57**, 110–121.



22. Yajnik CS, Deshpande SS, Jackson AA *et al.* (2007) Vitamin B<sub>12</sub> and folate concentrations during pregnancy and insulin resistance in the offspring: the Pune Maternal Nutrition Study. *Diabetologia* **51**, 29–38.
23. Valera-Gran D, García de la Hera M, Navarrete-Muñoz EM *et al.* (2014) Folic acid supplements during pregnancy and child psychomotor development after the first year of life. *JAMA Pediatr* **168**, e142611.
24. Whitrow MJ, Moore VM, Rumbold AR *et al.* (2009) Effect of supplemental folic acid in pregnancy on childhood asthma: a prospective birth cohort study. *Am J Epidemiol* **170**, 1486–1493.
25. Morton SMB, Ramke J, Kinloch J *et al.* (2015) Growing Up in New Zealand cohort alignment with all New Zealand births. *Aust N Z J Public Health* **39**, 82–87.
26. Morton SMB, Atatoa Carr PE, Grant CCC *et al.* (2013) Cohort profile: Growing Up in New Zealand. *Int J Epidemiol* **42**, 65–75.
27. Horsburgh SC, Malik M, Pauline N *et al.* (2009) *Prescribing and Dispensing Data Sources in New Zealand: Their Usage and Future Directions*. Dunedin: School of Pharmacy, University of Otago.
28. Ministry of Health (2006) *Food and Nutrition Guidelines for Healthy Pregnant and Breastfeeding Women: A Background Paper*. Wellington: Ministry of Health.
29. Statistics New Zealand (2009) *Final Report of Review of the Official Ethnicity Statistical Standard*. Wellington: Statistics New Zealand.
30. World Health Organization (2014) *Obesity and Overweight. Fact Sheet* no. 311. Geneva: WHO.
31. Brunner Huber LR (2007) Validity of self-reported height and weight in women of reproductive age. *Matern Child Health J* **11**, 137–144.
32. European Surveillance of Congenital Anomalies (2009) *Special Report: Prevention of Neural Tube Defects by Periconceptional Folic Acid Supplementation in Europe*. Belfast: EUROCAT.
33. de Walle HEK & de Jong-van den Berg LTW (2002) Insufficient folic acid intake in the Netherlands: what about the future? *Teratology* **66**, 40–43.
34. Bartholomew K, Morton SMB, Atatoa Carr PE *et al.* (2015) Early engagement with a lead maternity carer: results from Growing Up in New Zealand. *Aust N Z J Obstet Gynaecol* **55**, 227–232.
35. Ibrahim ZM, El-Hamid SABD, Mikhail H *et al.* (2011) Assessment of adherence to iron and folic acid supplementation and prevalence of anemia in pregnant women. *Med J Cairo Univ* **79**, 115–121.
36. Manniën J, de Jonge A, Cornel MC *et al.* (2014) Factors associated with not using folic acid supplements pre-conceptionally. *Public Health Nutr* **17**, 2344–2350.
37. Yi Y, Lindemann M, Colligs A *et al.* (2011) Economic burden of neural tube defects and impact of prevention with folic acid: a literature review. *Eur J Pediatr* **170**, 1391–1400.
38. Giroto F, Scott L, Avchalamov Y *et al.* (2013) High dose folic acid supplementation of rats alters synaptic transmission and seizure susceptibility in offspring. *Sci Rep* **3**, 1465.
39. Phelan S (2010) Pregnancy: a 'teachable moment' for weight control and obesity prevention. *Am J Obstet Gynecol* **202**, 135.e1–e8.
40. Atkinson L, Shaw RL & French DP (2016) Is pregnancy a teachable moment for diet and physical activity behaviour change? An interpretative phenomenological analysis of the experiences of women during their first pregnancy. *Br J Health Psychol* **21**, 842–858.
41. New Zealand Government (1985) Dietary Supplements Regulations 1985 (SR 1985/208). <http://www.legislation.govt.nz/regulation/public/1985/0208/latest/DLM102109.html> (accessed May 2017).
42. New Zealand Medicines and Medical Devices Safety Authority (2017) Product/Application Search. <http://www.medsafe.govt.nz/regulatory/DbSearch.asp> (accessed May 2017).
43. New Zealand Government (1981) Medicines Act 1981 (Public Act 1981 No 118). <http://www.legislation.govt.nz/act/public/1981/0118/latest/DLM53790.html> (accessed June 2017).
44. Hoffman DJ & Klein DJ (2012) Growth in transitional countries: the long-term impact of under-nutrition on health. *Ann Hum Biol* **39**, 395–401.
45. Organisation for Economic Co-operation and Development (2015) *Health at a Glance 2015: OECD Indicators*. Paris: OECD.
46. Williams J, Mai CT, Mulinare J *et al.* (2015) Updated estimates of neural tube defects prevented by mandatory folic acid fortification – United States, 1995–2011. *MMWR Morb Mortal Wkly Rep* **64**, 1–5.
47. Atta CAM, Fiest KM, Frolkis AD *et al.* (2016) Global birth prevalence of spina bifida by folic acid fortification status: a systematic review and meta-analysis. *Am J Public Health* **106**, e24–e34.
48. Ministry for Primary Industries (2012) Voluntary Folic Acid Fortification: Monitoring and Evaluation Report. MPI Technical Paper no. 2012/01. <https://www.mpi.govt.nz/dmsdocument/4163-voluntary-folic-acid-fortification-monitoring-and-evaluation-report> (accessed May 2017).
49. Australian Institute of Health and Welfare (2016) *Monitoring the Health Impacts of Mandatory Folic Acid and Iodine Fortification*. Canberra: Australian Institute of Health and Welfare.
50. Hilder L (2016) *Neural Tube Defects in Australia, 2007–2011: Before and after Implementation of the Mandatory Folic Acid Fortification Standard*. Canberra: Department of Health, Commonwealth of Australia.
51. New Zealand Ministry of Health (2018) *Folate Status of Women of Reproductive Age (15–49 Years). From the 2014/15 New Zealand Health Survey*. Wellington: Ministry of Health (In the Press).
52. Althubaiti A (2016) Information bias in health research: definition, pitfalls, and adjustment methods. *J Multidiscip Healthc* **9**, 211–217.
53. Green T, Newton R & Boum D (2003) Estimated folic acid intakes from simulated fortification of the New Zealand food supply. *N Z Med J* **116**, U294.
54. Evans SE, Mygind VL, Peddie MC *et al.* (2014) Effect of increasing voluntary folic acid food fortification on dietary folate intakes and adequacy of reproductive-age women in New Zealand. *Public Health Nutr* **17**, 1447–1453.
55. New Zealand Ministry of Health (2003) *Improving Folate Intake in New Zealand: Policy Implications*. Wellington: Ministry of Health.
56. Bradbury KE, Williams SM, Mann JI *et al.* (2016) Serum and erythrocyte folate status of New Zealand women of child-bearing age following a countrywide voluntary programme by the baking industry to fortify bread with folic acid. *Public Health Nutr* **19**, 2897–2905.
57. Lawrence M (2005) Assessing the case for mandatory folate fortification: policy-making in the face of scientific uncertainties. *Aust N Z J Public Health* **29**, 328–330.
58. Lawrence M & Riddell L (2007) Mandatory fortification with folic acid – what would Hippocrates say? *Aust Fam Physician* **36**, 69–70 72, 75.
59. Lawrence M (2005) Challenges in translating scientific evidence into mandatory food fortification policy: an anti-podean case study of the folate-neural tube defect relationship. *Public Health Nutr* **8**, 1235–1241.