Folate awareness and the prevalence of neural tube defects in South Australia, 1966–2007

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ABSTRACT

Objectives: To ascertain changes in: women's knowledge of the role of folic acid in the prevention of neural tube defects (NTDs); intake of folic acid among pregnant women; and prevalence of NTDs in South Australia.

Design, setting and participants: Computer-assisted telephone interviews of South Australian households from 1994 to 2007 over a period encompassing a statewide folate promotion campaign (1994–1995), continuing folate promotion, as well as the introduction of voluntary folate fortification of foods (1996); ascertainment of the total prevalence of NTDs from births and terminations of pregnancy from 1966 to 2007.

Main outcome measures: Changes in women's knowledge of the role of folic acid in the prevention of NTDs; changes in the prevalence of NTDs.

Results: From 1994 to 2006 and 2007, knowledge about the role of folic acid increased from 25% to 77% ($P < 0.001$) and knowledge that folic acid needs to be taken in the periconceptional period increased from 12% to 39% ($P < 0.001$). The proportion of pregnant women who increased their periconceptional intake of folate rose from 61% in 1998 to 81% in 2006 and 2007 ($P < 0.001$), with significant increases in the consumption of fortified cereals (from 15% to 29%) and folic acid tablets (from 37% to 64%). The total prevalence of NTDs fell from 2.06 per 1000 births in 1986–1990 to 1.23 per 1000 births in 2002–2007 (relative risk, 0.60; 95% CI, 0.48–0.74; $P < 0.001$).

Conclusions: Folate promotion and voluntary fortification of certain foods with folic acid were associated with increased awareness of the role of periconceptional folic acid, increased folate consumption and a reduction in the prevalence of NTDs in South Australia by 40% (95% CI, 26%–52%).

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Randomised controlled trials published in 1991 and 1992 from the United Kingdom[1] and Hungary[2] provided firm evidence that increased intake of folic acid in the periconceptional period — usually regarded as the month before pregnancy and the first 3 months of pregnancy — reduces the risk of having a baby with a neural tube defect (NTD) by about 72%. The Women's and Children's Hospital in Adelaide participated in the UK international trial, the results of which promised a rare opportunity for primary prevention of a group of severe birth defects.

Many countries started to promote periconceptional folate intake by informing women that their risk of having a baby with an NTD could be reduced if they consumed 0.4 mg of folic acid daily (or 0.5 mg, the content of the tablet in Australia) in the periconceptional period. The amount recommended is greater than the median amount of folic acid (0.2 mg) consumed daily by Australian women of reproductive age[3] and difficult to achieve by diet alone. Western Australia started promoting folate in 1992.[4] The South Australian campaign in October 1994 to August 1995, coordinated by the Women's and Children's Hospital and the South Australian Department of Health (SA Health), provided information about folate and the prevention of NTDs to health professionals and the community.[5]

In 1995, voluntary fortification of specified foods with folic acid was approved in Australia, allowing up to 50% of the recommended daily intake of folic acid (ie, 0.1 mg) to be added per reference quantity (generally, a normal serving or equivalent specified quantity). From 1996, increasing numbers of foods were fortified with folic acid, mainly breakfast cereals, fruit juices and milk. The Women's and Children's Hospital has continued to distribute folate information sheets and has a folate telephone message, and occasionally disseminates newspaper and television messages. The personal health record provided by child health services for each baby at birth and SA Health's pregnancy information website (http://www.health.sa.gov.au/PREGNANCY/DesktopDefault.aspx?tabid=45) also contain information about folate. The Australian Government began promoting folate in September 1997.

In this report, we document changes in knowledge about folic acid's role in the prevention of NTDs among women of reproductive age, and changes in the prevalence of NTDs in a state with a previously stable total prevalence in 1966–1991.[6]

METHODS

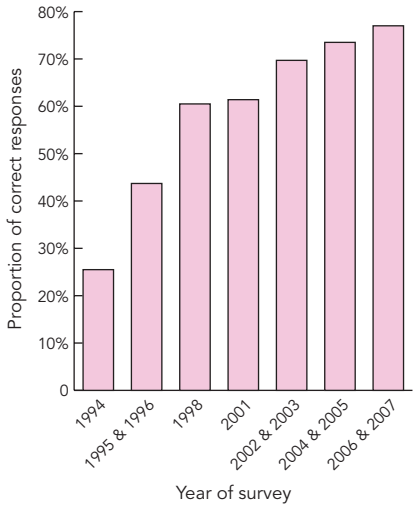
South Australia has a population of 1.6 million, and recorded about 18 500 births a year in 1994–2007.

Folate awareness

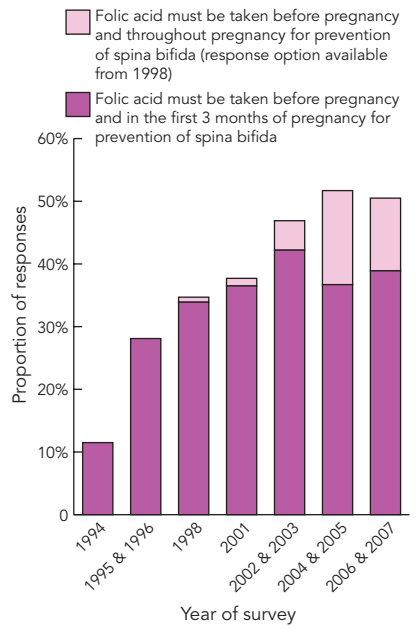
We obtained folate awareness data from women of reproductive age (18–50 years) in a series of SA Health computer-assisted telephone interview (CATI) surveys, through random dialling of South Australian telephone numbers obtained from the electronic White Pages (97% of South Australian households have a telephone). These surveys had two questions in common. From 1998, women surveyed who were pregnant or had given birth within the preceding 3 years were asked whether they had increased their intake of folate-rich foods, or consumed cereals fortified with folic acid, or consumed folic acid tablets daily for that (or the most recent) pregnancy "in the month before you became pregnant" and "in the first three months of pregnancy". (A copy of the questionnaire used in the interviews is available on request.) These surveys are listed below.

- Surveys of about 400 women of reproductive age in each year from 1994 to 1996 to evaluate the "Folate before pregnancy" promotion campaign.
- A 1998 survey involving 2077 women, including 292 who were pregnant or had given birth in the preceding 3 years.[7]
- A 2001 survey of 923 women, including 159 who were pregnant or had given birth in the preceding 3 years.[8]
- The South Australian Monitoring and Surveillance System (SAMSS), implemented by SA Health in July 2002 to monitor population trends in key health issues on a regular monthly basis through about 600

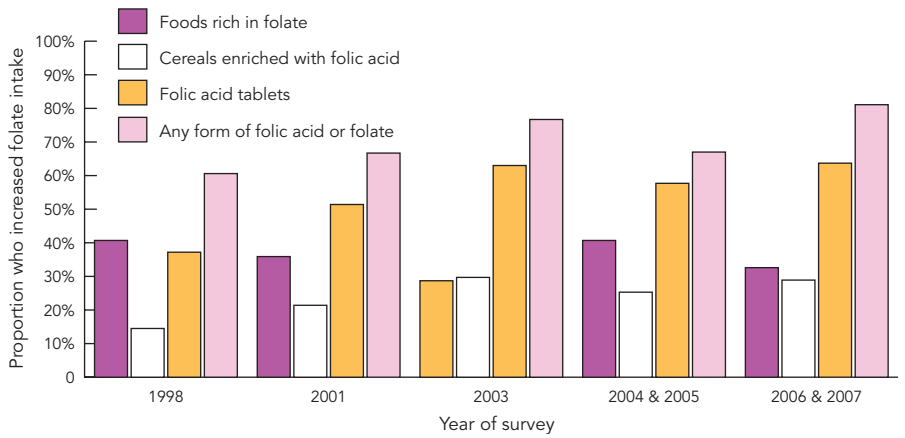
1 Knowledge that folate may prevent spina bifida if enough is taken by the mother, among women of reproductive age, South Australia, 1994–2007



2 Knowledge of the timing of folate supplementation among women of reproductive age, South Australia, 1994–2007



3 Increase in folate intake and source of increased intake among women who had been pregnant within the previous 3 years, South Australia, 1998–2007



CATI interviews per month[9] (509–730 women in the reproductive age group each year in the years 2003–2007).

Prevalence of neural tube defects

Pregnancies resulting in births of babies with NTDs were ascertained from the South Australian perinatal data collection of births (live births and stillbirths of at least 400 g birthweight or 20 weeks' gestation), which have been required to be notified to SA Health under legislation since 1986. Terminations of pregnancy for NTDs were ascertained from notifications under specific abortion legislation introduced in 1970.[6] The South Australian Birth Defects Register[10] collates all these data, including rare cases detected late (before the child's fifth birthday). Cases of NTDs are validated through review of perinatal and postneonatal death certificates; medical, ultrasound, maternal serum screening, cytogenetics and autopsy reports; and, where necessary, case records and consultation with the clinicians and/or pathologists involved.

Ethical approval

Formal approval for this study was sought and obtained from SA Health's Human Research Ethics Committee.

RESULTS

Folate awareness

The response rate in the CATI surveys ranged from 65% to 75%. Box 1 shows that the proportion of women of reproductive age who were aware of the role of folic acid in the prevention of NTDs (specifically, spina bifida) increased from 25.5% in 1994 to 77.0% in 2006 and 2007 (χ^2 test for trend for individual years, 432.76; $P < 0.001$). Box 2 shows that the proportion of women who knew that folate should be taken before pregnancy and in the first 3 months of pregnancy for prevention of spina bifida increased from 11.5% in 1994 to 38.9% in 2006 and 2007 (χ^2 test for trend, 69.60; $P < 0.001$). As a few women in the surveys in earlier years responded "before and throughout pregnancy", this response option was available from 1998 and is shown in Box 2.

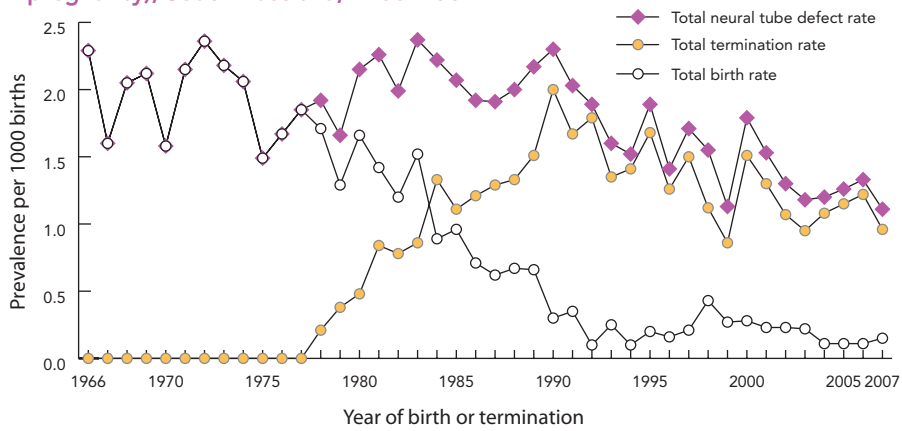
Box 3 shows that, among women who were pregnant or who had recently given birth, an increasing proportion increased their daily consumption of any form of folate in the periconceptional period, from 60.6% in 1998 to 81.1% in 2006 and 2007 (χ^2 test for trend, 18.74; $P < 0.001$). The proportion who consumed cereals fortified with folic acid increased from 14.5% to 28.9% (χ^2 test for trend, 15.14; $P < 0.001$) and those consuming folic acid tablets increased from 37.2% to 63.7% (χ^2 test for trend, 33.66; $P < 0.001$). However, the proportion who increased their intake of folate-rich foods showed no significant trend during this period, from 40.7% to 32.6% (χ^2 test for trend, 1.53; $P = 0.22$).

Prevalence of neural tube defects

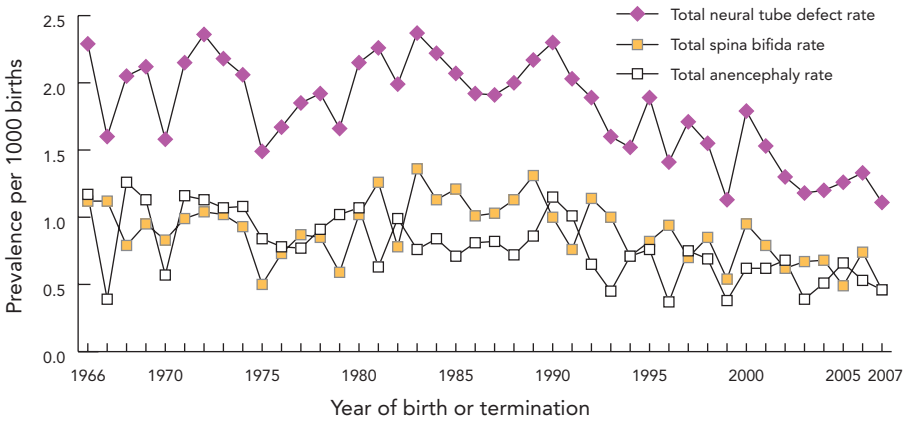
Box 4 and joinpoint analysis (Joinpoint Regression Program, version 3.3; Statistical Research and Applications Branch, National Cancer Institute, Bethesda, Md, USA) show that the prevalence of all NTDs in South Australia was stable between 1966 and 1990 and declined significantly thereafter (Poisson regression 1966 to 2007, $P < 0.001$). Box 5 shows that this decline also applied individually to anencephaly ($P < 0.001$) and spina bifida ($P < 0.01$).

Folate promotion and the implementation of voluntary fortification of some foods from 1996 was associated with a decrease of 40% (95% CI, 26%–52%) in the total prevalence of NTDs in South Australia, from 2.06 per 1000 births in 1986–1990 (before any

4 Prevalence of neural tube defects (total, births and terminations of pregnancy), South Australia, 1966–2007



5 Prevalence of total neural tube defects, spina bifida and anencephaly, South Australia, 1966–2007



statewide folate promotion, when there were 40–41 cases per year) to 1.23 per 1000 births in 2002–2007 (average of 22–23 cases per year; relative risk [RR], 0.60; 95% CI, 0.48–0.74; $P < 0.001$). Over the same period, the reduction in prevalence of anencephaly was 38% (RR, 0.62; 95% CI, 0.44–0.86) and of spina bifida was 44% (RR, 0.56; 95% CI, 0.41–0.75).

DISCUSSION

From the first CATI survey results in 1994, it appears that there was already some community knowledge about folate before the promotion campaign that commenced that year. However, the surveys show that folate promotion from many sources and the introduction of voluntary folic acid fortification have been associated with a significant increase in the proportion of women of reproductive age in South Australia who know about the role of folate in the prevention of NTDs and when folate must be consumed. Among women pregnant in the preceding 3 years, there was also a significant increase in the consumption of cereals fortified with folic acid, folic acid tablets, and in the consumption of any form of folate.

These CATI surveys have several limitations. They are affected by recall bias among women who are or were recently pregnant in reporting what they consumed in the periconceptional period. Further, the numbers of questions were limited, which restricts in-depth exploration of issues, and there was no possibility of validating the responses. Although the results of the CATI surveys were age-adjusted to the state population, the surveys may have overestimated knowledge and compliance, as women aged under 18 years were not interviewed and there may have been self-selection of more knowledgeable women in responding. In addition, women were not asked for details of the types of food or folic acid tablets consumed. Serum and red blood cell folate levels were also not determined.

Two studies of folic acid intake among pregnant women attending clinics at teaching hospitals in Adelaide have been undertaken.[11,12] They showed lower levels of full compliance with the consumption of folic acid tablets in the periconceptional period than did the CATI surveys of the population — 31% in 1999[11] and 30% in 2005.[12] However, an additional 13% of women in 1999[11] and 43% in 2005[12] reported that they had tried to comply, but took lower-dosage tablets or did not take tablets for the full period. The levels of knowledge and use of folic acid supplements were high in these young pregnant public patient populations. The 1998 CATI survey, which asked about the type of folic acid tablets, also showed that some women took tablets (usually multivitamins) containing less than 0.4 mg of folic acid.[7] Many of these women may have achieved an adequate daily level of 0.4 mg by consuming fortified cereals or increasing their intake of folate-rich foods.

The CATI surveys showed that folate awareness was lower among women from non-English-speaking countries, those residing in rural areas and those with low household income.[7-9] Studies elsewhere have also shown that knowledge is associated with older age, non-immigrant status, higher education, marriage, and planned pregnancy.[13] It is estimated that over 40% of pregnancies in many countries are unplanned,[5,13] and evaluations performed after folate promotion projects have found that not more than 50% of women are taking periconceptional folic acid supplements.[4,13]

The strengths of our study lie in the consistent methods and response rates of the CATI surveys, and the total population coverage. Another major strength is South Australia's ability to derive the total prevalence of NTDs through both births and terminations of pregnancy, and the thoroughness with which this is achieved. However, for the reasons given above, the surveys may have slightly overestimated the levels of and improvements in knowledge and practice of folate supplementation.

Almost no decline in total prevalence of NTDs has been observed in most European countries after folate promotion projects.[13] However, in South Australia, with folate promotion from many sources and voluntary fortification, the total prevalence fell by 40% between 1986–1990 and 2002–2007.

Mandatory fortification has now been implemented in over 40 countries. It has been associated with falls in the prevalence of NTDs in Canada (46%, ranging from 22% to

83% in different provinces),[14] Chile (31%),[15] Costa Rica (35% among births)[16] and in the United States (20% to 32%, from several monitoring programs).[17] In the US, mean daily food and total folate intake increased by about 0.1 mg per day after fortification. Among women of reproductive age, 26% to 39% (varying by race or ethnicity) achieved more than 0.4 mg daily intake of folate.[17]

While some have called for higher levels of fortification with folic acid[18,19] and additional fortification with vitamin B_{12},[18] others have recommended a more cautious approach,[20] advising that significant reductions have already been achieved in the prevalence of low levels of serum and red-cell folate. Moreover, monitoring programs with better case ascertainment have shown a 50% reduction in prevalence of NTDs after mandatory food fortification with folate;[21] a lack of data on terminations of pregnancy to determine total NTD prevalence may result in underestimates of effect. The amount by which NTD prevalence can be reduced is also dependent on the initial prevalence[14,22] and on the proportion of folate-responsive cases.[23]

We look forward in Australia to a further reduction in NTD prevalence with mandatory food fortification, which was gazetted in September 2007 and will be enforceable in September 2009.[24] It is unlikely that reduction beyond a residual level of about 0.6 NTD-affected fetuses per 1000 births can be achieved, this being the lowest level achieved internationally.[22,25] There are also needs to monitor safety, including possible effects on those on anti-folate therapy, to monitor other effects such as those on cardiovascular disease risk and cancer, and issues surrounding fortification of foods with vitamin B_{12}.

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COMPETING INTERESTS

None identified.

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