U.S.A. and Canada:

Public health improvements from increased folic acid consumption

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CDC-Atlanta

Neural tube defects

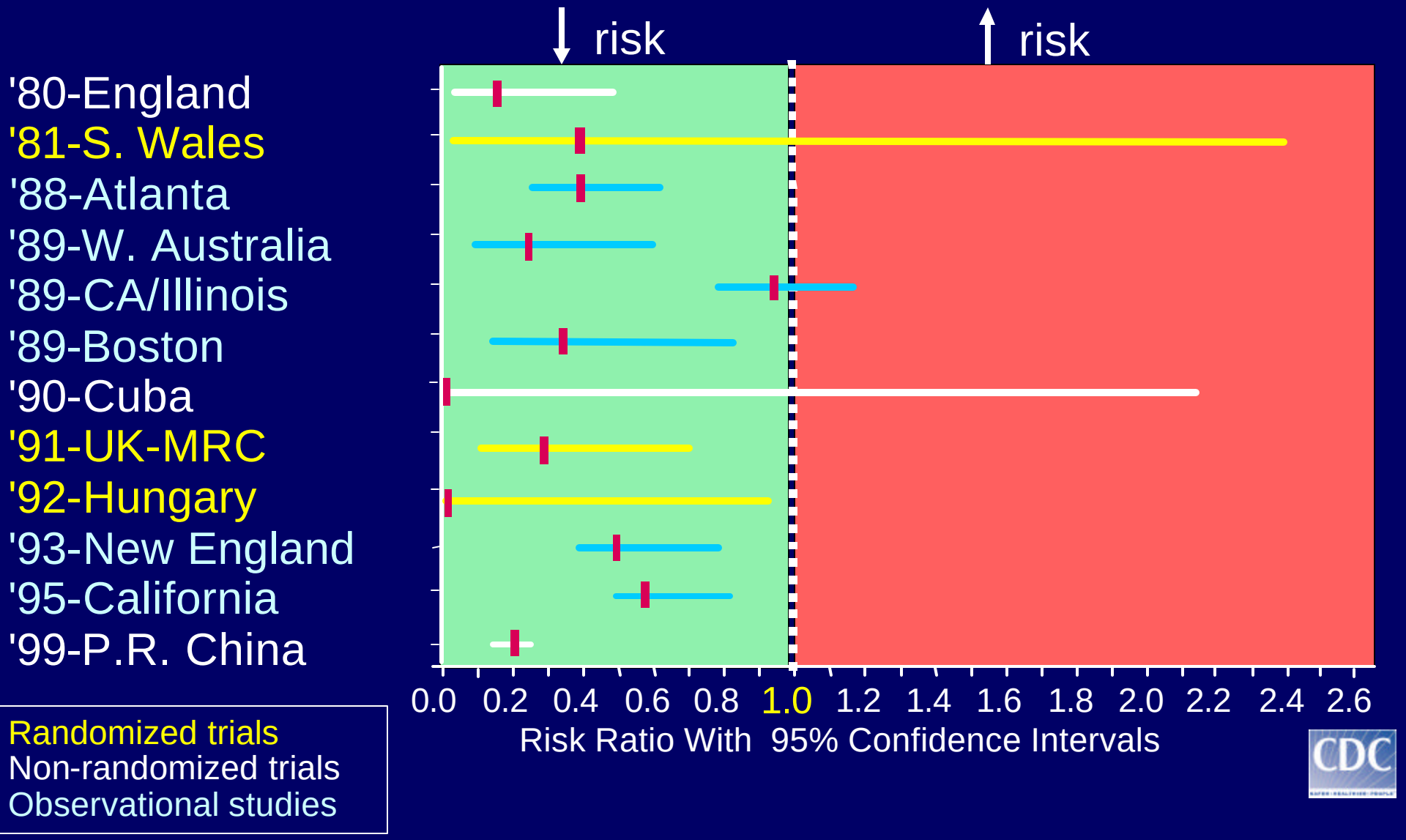
- Serious birth defects
  - spina bifida and anencephaly
- > 1 of 1000 pregnancies
- > 300,000 yearly worldwide

- Increased consumption of folic acid can prevent 50-80%

- Comprehensive, robust data
  - Randomized controlled trials
  - Consistent case-control studies
  - Occurrence and recurrence
  - Both multivitamins and folic acid alone
  - Consistent genetic findings (MTHFR)

CDC

Multivitamins with Folic Acid
Neural Tube Defect Studies, 1980-1999



What has been done to increase folic acid consumption in US?

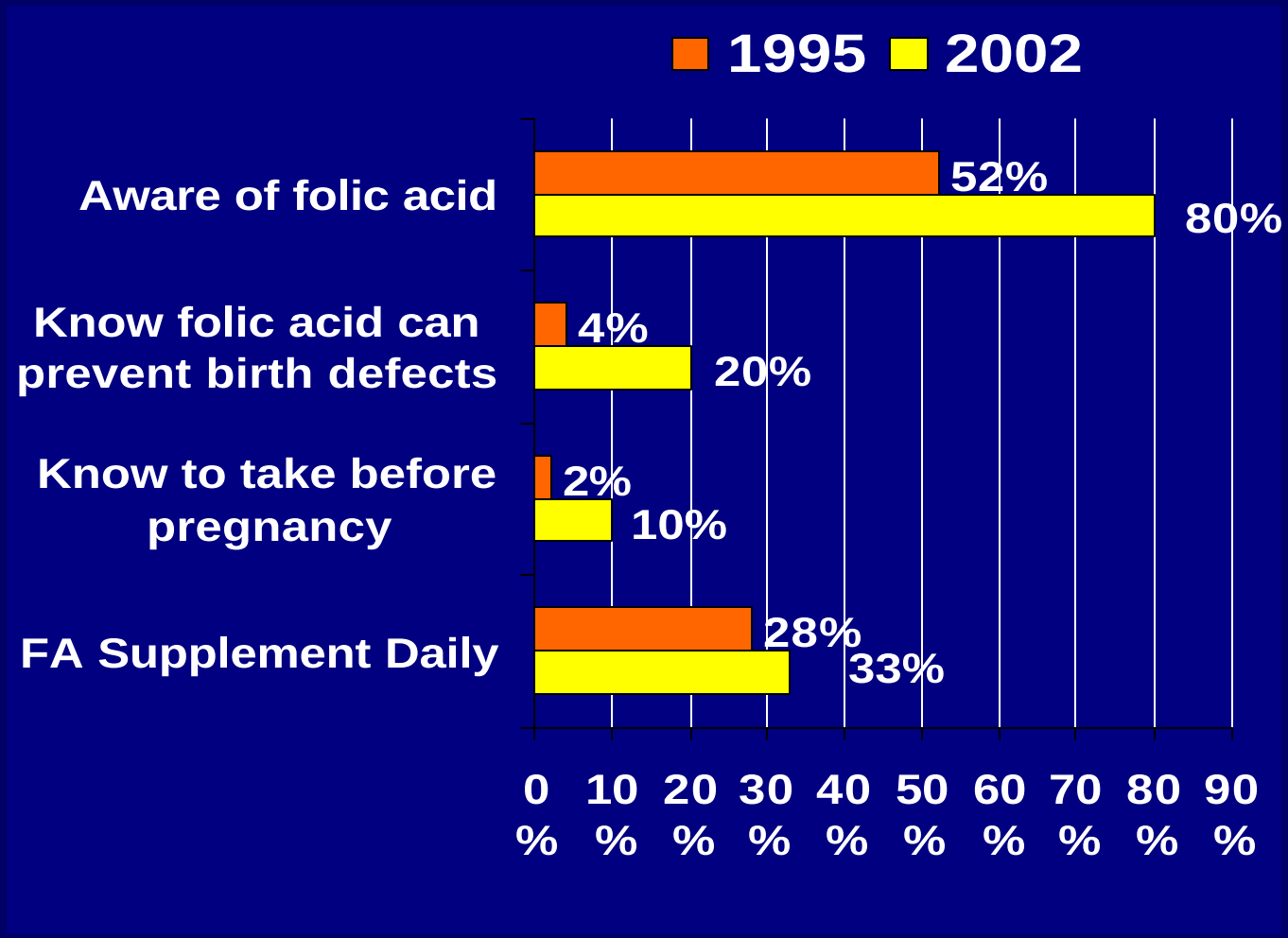
- FDA mandates that all products made with “enriched” flour or grain products contain additional folic acid, 140 ug/100g (design consumption = 100 ug/day)
- FDA approves the use of health claims on products that contain “significant” amounts of folic acid
- Supplement-use health communications by many groups, notably the March of Dimes
- Breakfast cereal manufacturers add folic acid to many products

Supplements

- **Canada:** available, multivitamins, 200-400 µg FA

- **USA:** widely available multivitamins, most 400 µg FA; (prenatals 800-1000 µg FA); (breakfast cereals, many 400 µg FA)

USA: Awareness and Usage of Folic Acid MOD Surveys 1995, 2002



March of Dimes

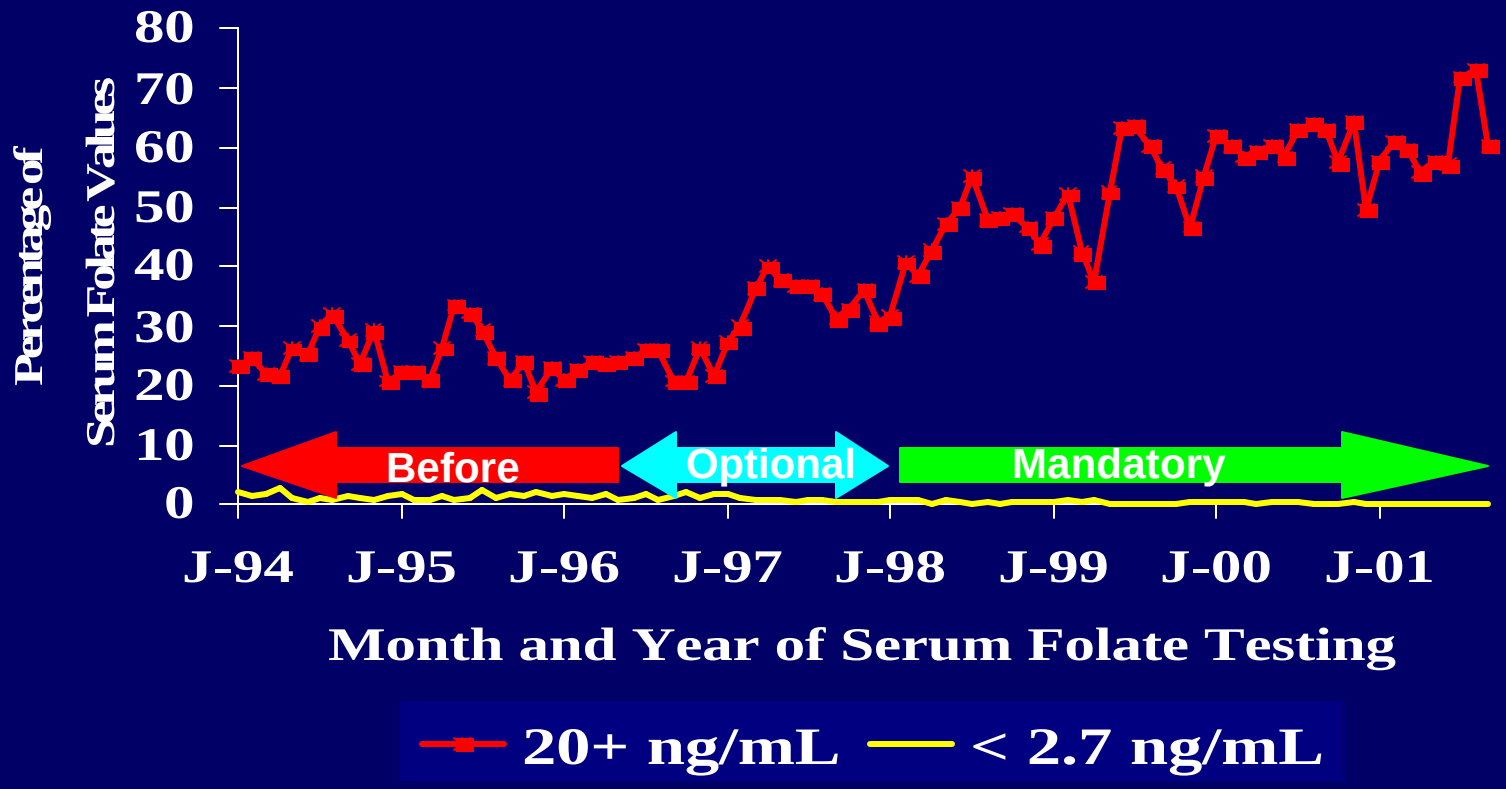
CDC

Fortification

- **Canada 1998:** cereal grain flours, 150 µg FA per 100 g flour – design 100 ug / day
- **Chile 2000:** wheat flour, 220 µg FA per 100 g flour – design 400 ug / day
- **USA 1998:** wheat, corn, rice flours, 140 µg FA per 100 g flour – design 100 ug / day
- **Most other countries:** laws, little action

Blood Folate Changes

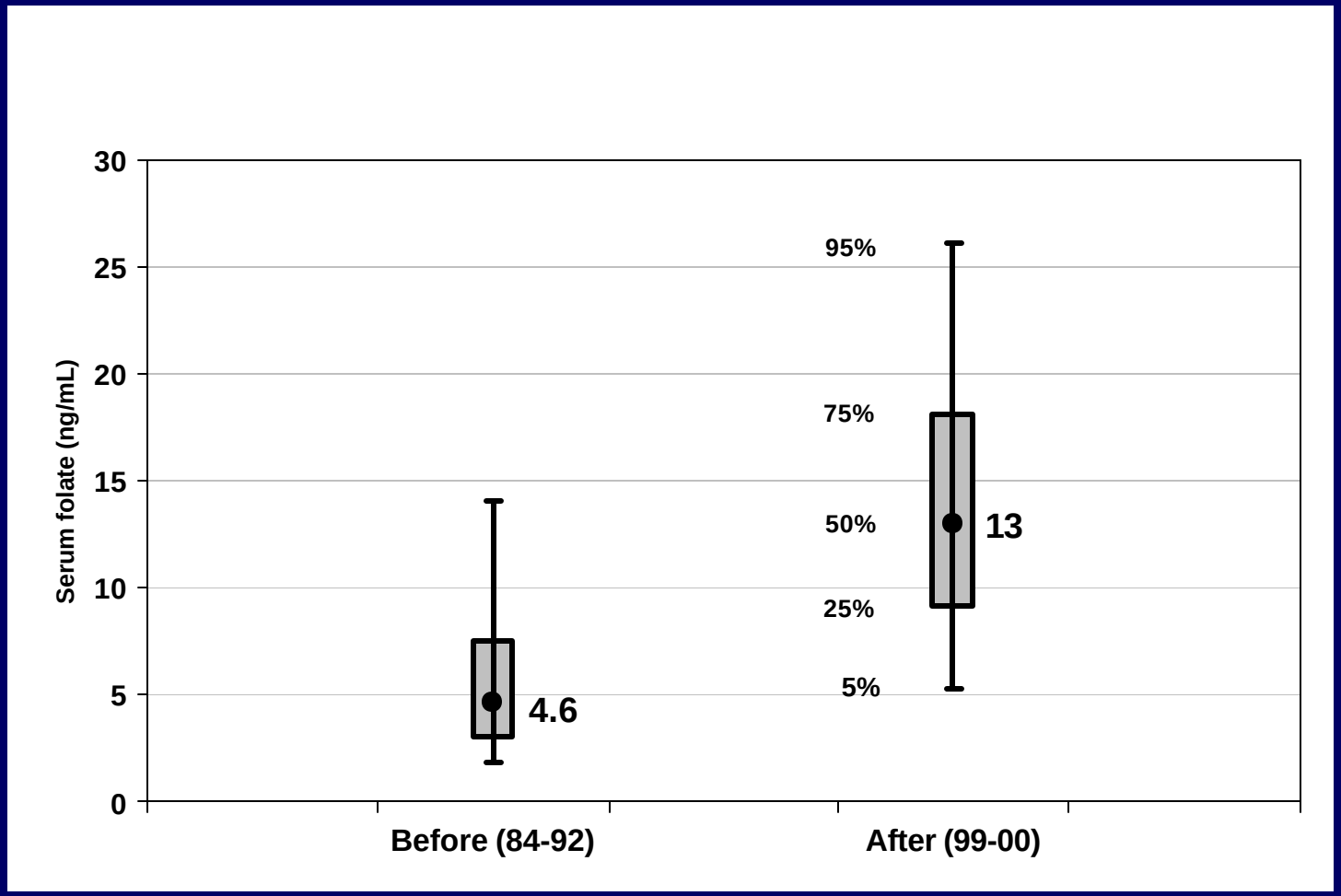
Percentage of Serum Folate Values from Kaiser Permanente Southern California Patients
< 2.7 ng/mL and ³ 20 ng/mL, by Month, 1994-2001



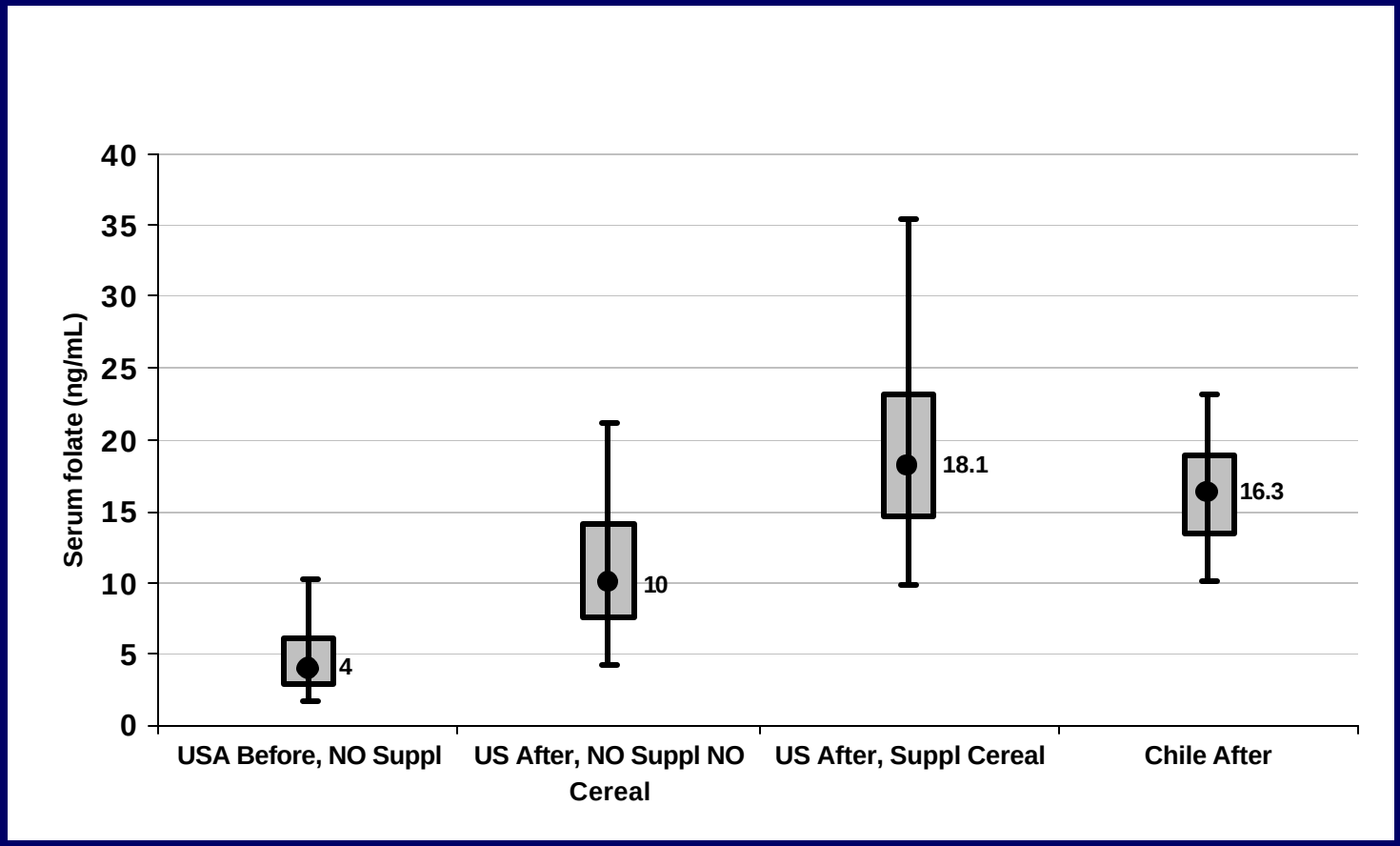
Lawrence JM, Petitti DB, Watkins M, Umekubo MA. Trends in serum folate after food fortification. Lancet 1999;354:915-6.
Lawrence JM, Chiu V, Petitti DB. Fortification of Foods with Folic Acid [Letter]. NEJM 2000; 343: 970.

Data for 2000 and 2001 added since publication Data for 2001 is from January through September, 2001. (12/4/01)

USA: Serum folate among non-pregnant women aged 15-44 years before and after flour fortification (NHANES 88-92, and 00-99)



USA: Serum folate among non-pregnant women aged 15-44 years by supplement and cereal use, before and after fortification, and Chile after



Canada (Ontario): Red Blood Cell Folate, Serum Vitamin B12, Before and After Fortification, Women 18-42

	Before	After	Change
RBC folate, ng/ml mean	239	337	97(41%)
RBC folate 5th %tile	118	182	64(54%)
Se B12, pmol/L mean	276	270	-6(-2%)
Se B12 5th %tile	125	130	+5(=4%)

Neural Tube Defect Changes

US – NBDPN
Change in NTD prevalence*
(24 programs)

	Pre-fort.	Optional fort.	Mandatory fort.	PR** (95% CI)	% decline
Spina bifida	5.14	4.28	3.47	0.67 (0.63-0.73)	33%
Anencephaly	2.45	2.11	2.11	0.86 (0.78-0.95)	14%

* Prevalence per 10,000

**Compares mandatory to pre-fortification prevalence

Table 1: Annual incidence of open neural tube defects* (NTDs) in Nova Scotia before folic acid supplementation (1991–1994), after supplementation but before folic acid fortification (1995–1997) and after fortification (1998–2000)

Year	No. of cases of open NTDs: In live births and stillbirths	No. of cases of open NTDs: In terminated pregnancies	No. of cases of open NTDs: Total	Total no. of births†	Incidence per 1000 births
Pre-supplementation					
1991	18	12	30	11 933	2.51
1992	17	13	30	12 076	2.48
1993	14	16	30	11 715	2.56
1994	12	18	30	11 340	2.64
Post-supplementation/ Pre-fortification					
1995	5	18	23	10 913	2.11
1996	13	25	38	10 739	3.54
1997	8	14	22	10 125	2.17
Post-fortification					
1998	7	7	14	9 785	1.43
1999	1	10	11	9 676	1.14
2000	1	8	9	9 549	0.94
Total	96	141	239	107 851	2.22

*Includes spina bifida, anencephaly and encephaloceles.
†Live births, stillbirths and pregnancies terminated because of fetal anomalies.

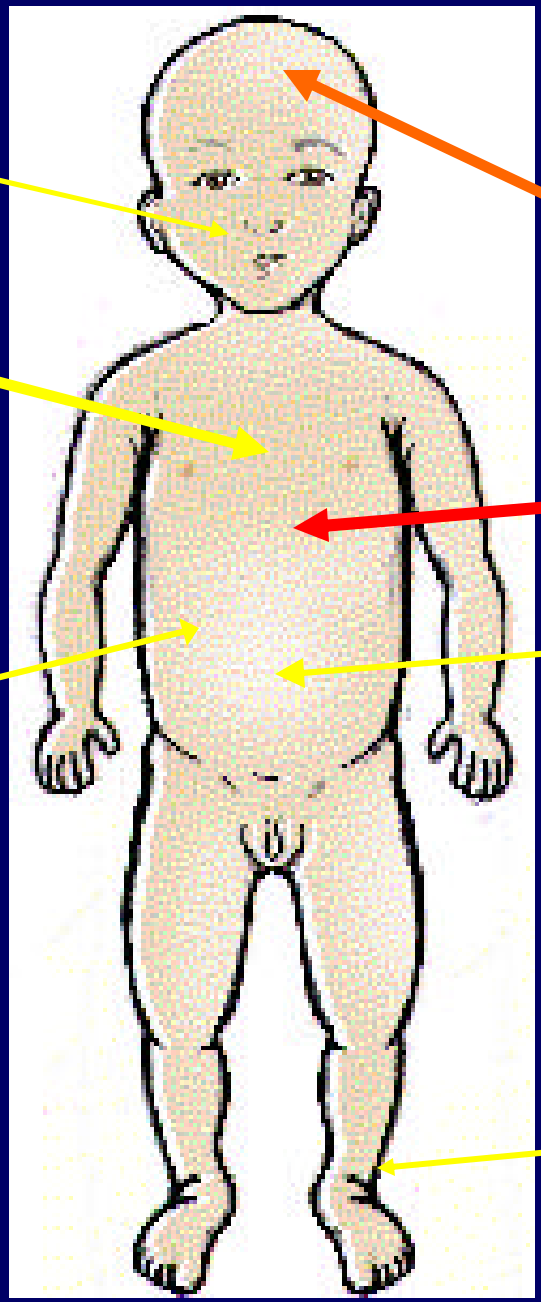
Persad et al: Can Med Assoc J, Volume 167(3).August 6, 2002.241-245

Are Other Birth Defects Prevented by Folic Acid/Multivitamins?

Cleft lip/palate
(Cleft palate)

Heart defects:
- Conotruncal
- VSD
- Possibly others

Urinary tract ?



Anencephaly
Spina bifida

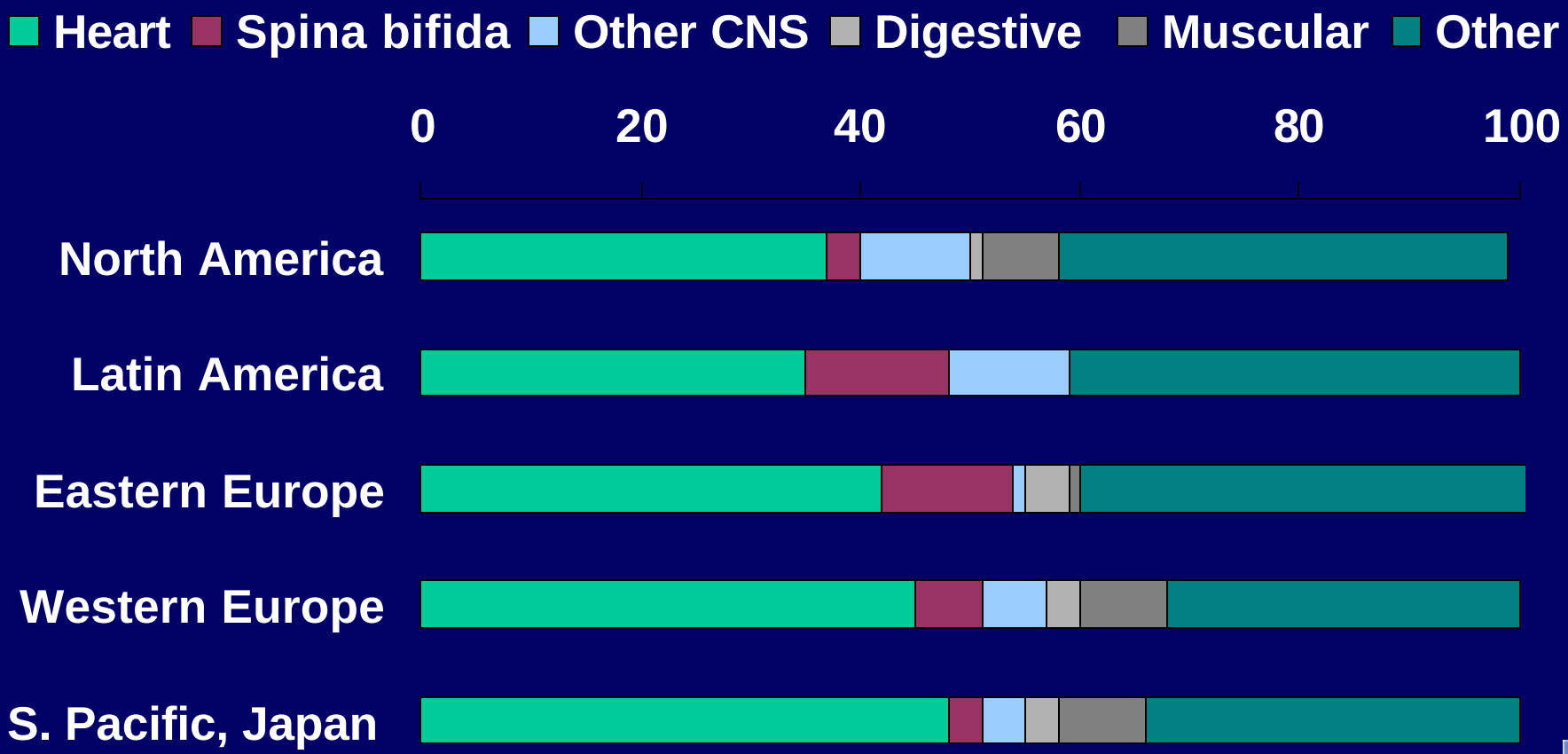
Omphalocele ?

Limb deficiency
- type?

Congenital anomalies vs. MV/folic acid

CDC

Non-NTD birth defects cause most infant deaths due to congenital anomalies (heart defects are a leading cause)



Source: J Epidemiol Comm Health 2000;54(9):660-6 (WHO, 1990-1994)

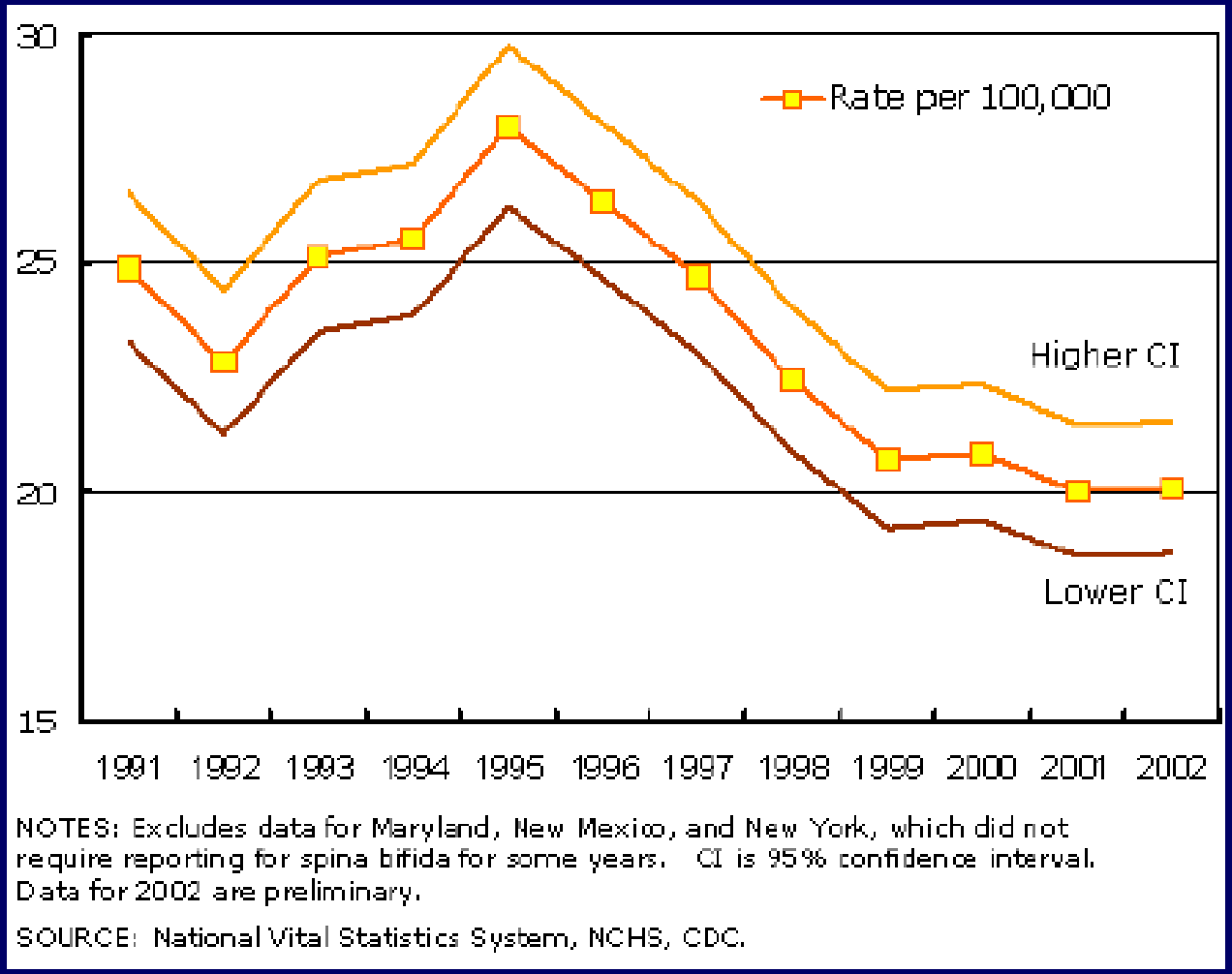
Neural tube defects

- Serious birth defects
  - spina bifida and anencephaly
- > 1 of 1000 pregnancies
- > 300,000 yearly worldwide

- Increased consumption of folic acid can prevent 50-80%

- Prevention through fortification

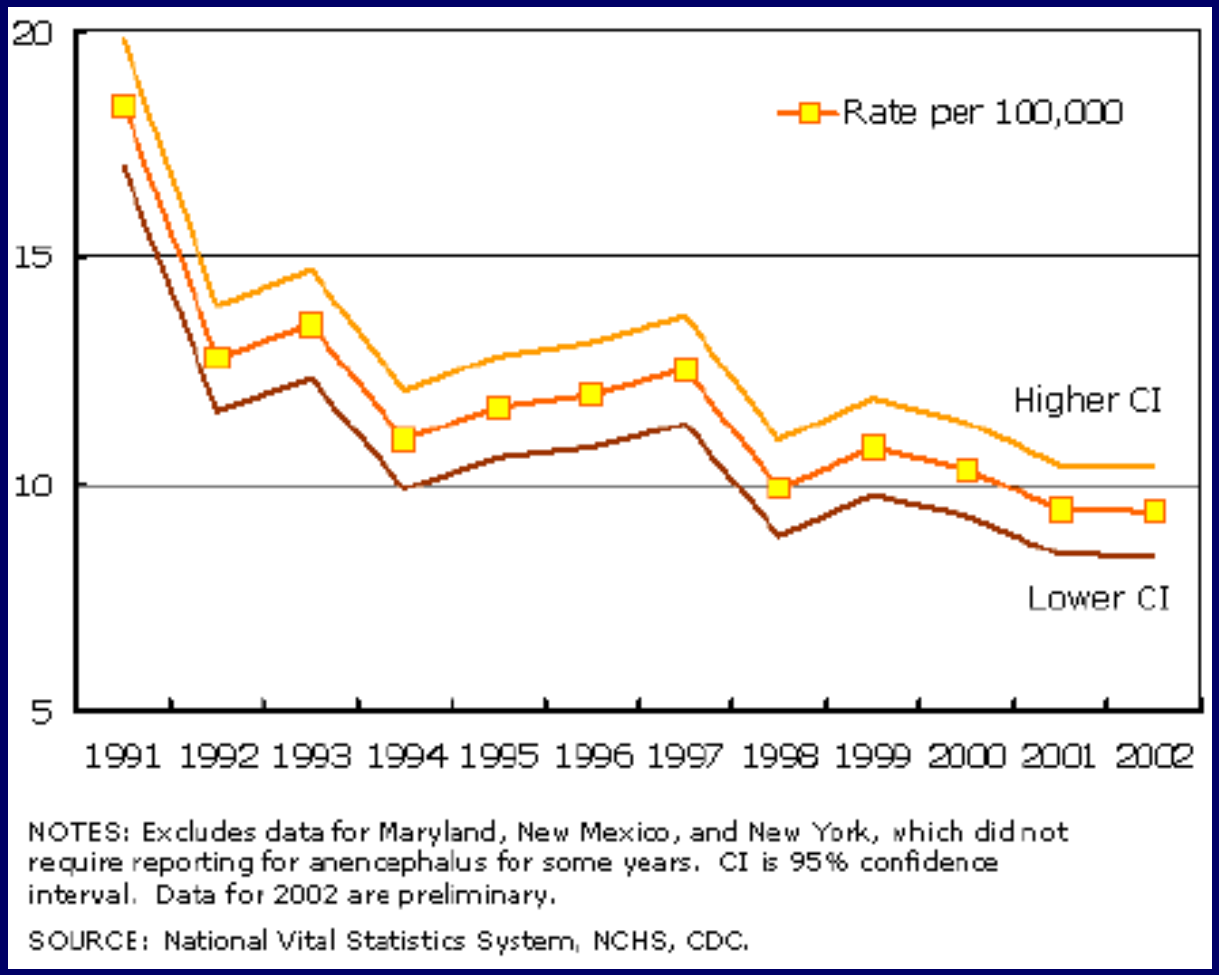
Spina Bifida Rates, Live Births USA



NOTES: Excludes data for Maryland, New Mexico, and New York, which did not require reporting for spina bifida for some years. CI is 95% confidence interval. Data for 2002 are preliminary.

SOURCE: National Vital Statistics System, NCHS, CDC.

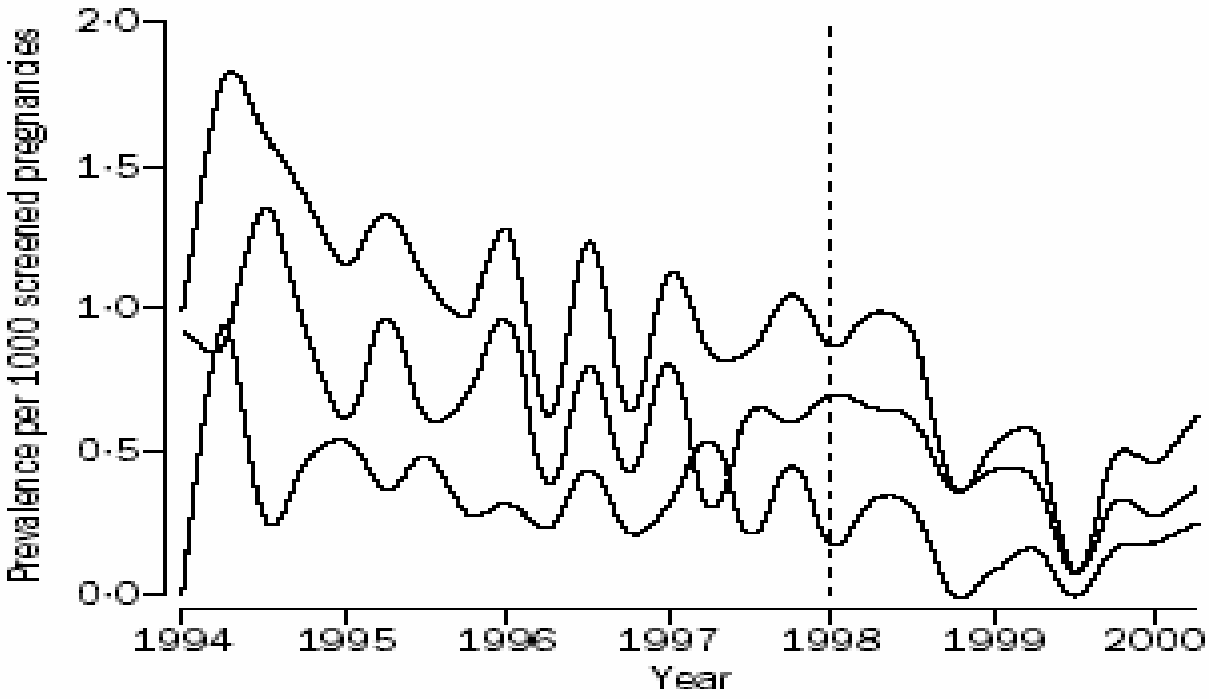
Anencephaly Rates, Live Births USA



NOTES: Excludes data for Maryland, New Mexico, and New York, which did not require reporting for anencephalus for some years. CI is 95% confidence interval. Data for 2002 are preliminary.

SOURCE: National Vital Statistics System, NCHS, CDC.

NTD Rates Before and After FA Fortification, ONTARIO

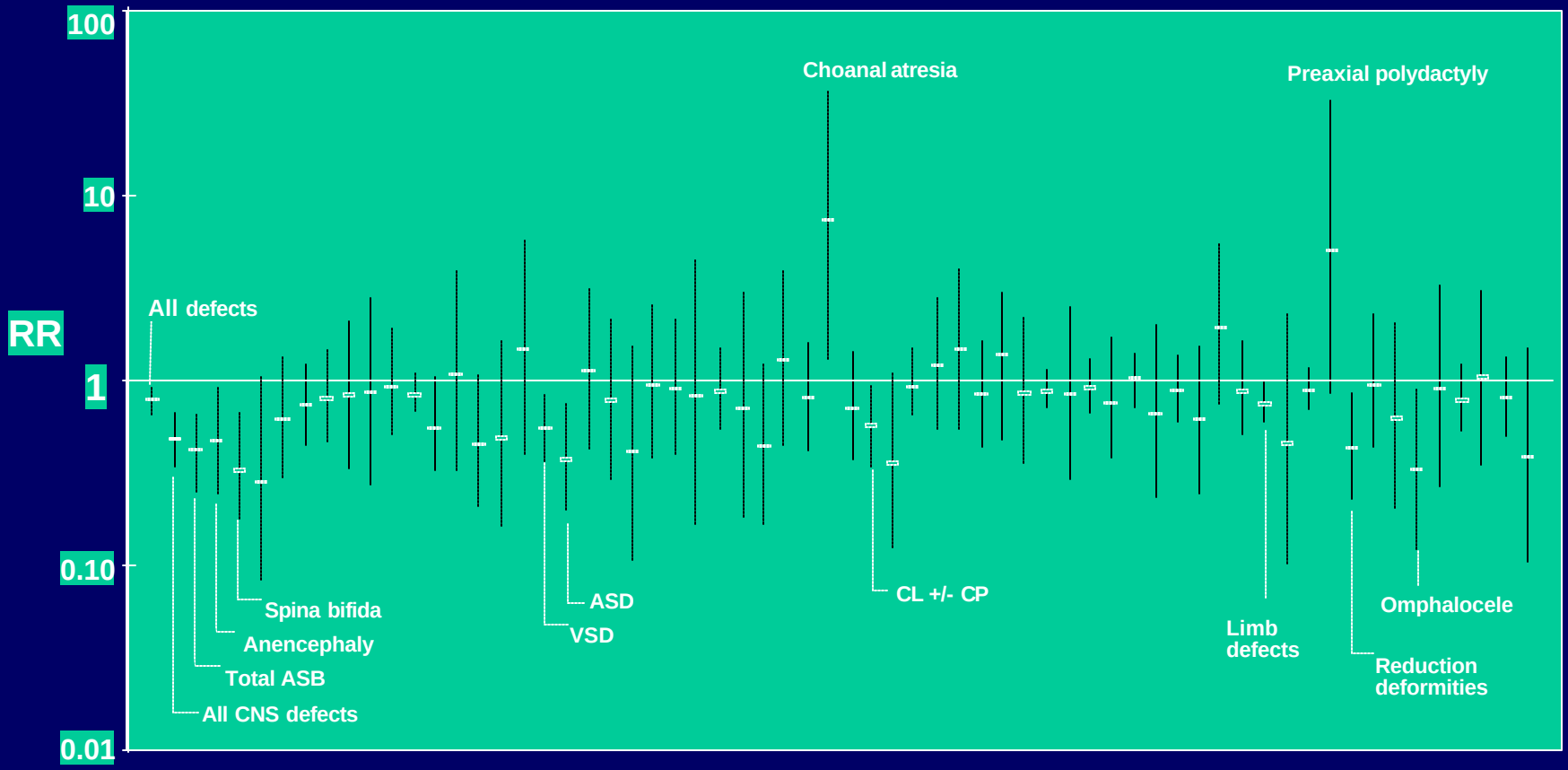


Quarterly prevalence of open neural tube defects (upper), spina bifida (middle), and anencephaly (lower) before and after (vertical dashed line) folic acid food fortification

Ray et al Lancet 2002

Estimated relative risks (RR) of the association between reported periconceptional multivitamin use and the occurrence of selected birth defects

ABDCCS, 1968-1980



Selected Birth Defects